The influence of cannabis on driving

Prepared for Road Safety Division, Department of the Environment, Transport and the Regions

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Results from the study of the 'Incidence of alcohol and drugs in road accident fatalities' have consistently shown a large increase in the incidence of drugs in fatal road casualties (drivers, riders, passengers and pedestrians) since the last comparable study in the mid-1980s. The latest results show that among all road users traces of illicit drugs were present in 18% of fatalities. These figures represent a six-fold increase in presence of illicit drugs when compared with the previous study (Everest, Tunbridge and Widdop, 1989). Cannabis constitutes around two thirds of the illegal drugs found.

Despite the increase in the incidence of drugs, it is not possible to say that drugs caused these deaths. There may be an association, but presence cannot be taken as evidence of causation - there is no way of telling how much was consumed and how long before the fatal accident. So far as cannabis is concerned, the prevalence in drivers was not significantly different from that of passengers, who can be taken as a (albeit imperfect) measure of the prevalence in the population as a whole. However, cannabis remains detectable in the body for up to four weeks after use - long after any impairment of driving.

In addition, in most surveys reported in Europe cannabis is the most frequently detected illicit drug (de Gier, 1998). In a range of accident involved populations cannabis is found with an incidence between 2 and 12% with a mode incidence around 5-8%. This is certainly significantly above that of any other illicit drug.

Previous research studies on cannabis and driving have focused largely on the effects of cannabinoids on driving performance. These studies have been almost exclusively experimental, involving laboratory tasks, driving simulator and on road 'real driving' experiments. A much smaller number of studies have attempted to gain broader sociological information about driving habits under the influence of cannabis and what factors influence the decision to drive. This research attempts to combine these two aspects, certainly for the first time in the UK, with a view to assessing the degree to which there may be a problem with cannabis in relation to driving. The research has three primary objectives:

- To provide reliable data, under laboratory conditions, on the impairing effects of cannabis on driving.
- To determine the duration and extent of any impairment under different degrees of intoxication (using different levels of cannabis).
- To provide an overview of attitudes and habits of cannabis users in relation to driving and explore factors which may influence the decision to drive under its influence.

The research attempted to address these objectives using experienced cannabis users carrying out a variety of laboratory-based tasks and driving in a driving simulator under four cannabis conditions: placebo; low THC; high THC; and cannabis resin. The placebo, low and high dose THC conditions used herbal cannabis ('grass') cigarettes supplied by the National Institute on Drug Abuse (NIDA), while the cannabis resin condition used cannabis supplied by Customs and Excise from seized supplies.

In 1999 DETR commissioned a review (Ward & Dye, 1999) of the latest evidence of the impairment effects of cannabis. That report provided an overview of the effects of cannabis on driving and accident risk and identified key research questions for areas where current knowledge was deemed to be insufficient to guide road safety policy. These research questions have shaped and informed the current research project. In addition to the primary objectives outlined above, the research reported here sought to inform four key issues identified by the Ward and Dye report.

These were: exposure; biological response; acute psychomotor response; and driving response.

i Exposure

Prior to this research, few studies have attempted to gain broader sociological information about driving under the influence of cannabis. A comparison between the participants in the current study and a group of regular users in the West Midlands showed the trial group to be fairly typical. Both groups showed a reluctance to drive after consuming more than 4 units of alcohol, believing their driving to be significantly impaired. The majority of both groups again thought that cannabis impaired their driving, but only to a slight degree.

ii Biological response

In considering the results of the present study, the biological response of the participants to the consumption of cannabis is of fundamental importance. Urine was screened on arrival to check for and exclude multiple drug use.

Blood and saliva measurements were taken immediately prior to dosing and at 10 and 30 minutes post dosing. The subjective reports given by the participants of the effects of smoking the various strengths of cannabis cigarettes showed an extremely good correlation between what participants thought they had smoked and the THC dosage in the cigarettes. The maximum amounts of THC administered were around 10mg for the low dose and 20 mg for the high and the majority of participants were able to distinguish between the effects of these doses and placebo. The subjective feelings of the 'highs' experienced were also closely correlated with the participants 'liking' of the smoking effect as stated in the mood questionnaire. Making allowance for the experimental situation, the majority of participants also found the experience of smoking cannabis similar to their normal experience.

iii Acute psychomotor response and tests of impairment

It is of the utmost importance to try to relate the observations derived from this experimental study to the situations likely to be encountered in real life drug driving

cases. Part of the experimental procedures therefore included the formal sobriety testing of participants. Two registered medical practitioners (experienced Forensic Medical Examiners (FMEs)) examined the participants and carried out a comprehensive physical examination to see whether the suggested standard 'impairment' tests currently used were effective in detecting impairment due to cannabis.

The results of the sobriety testing clearly show a strong correlation between cannabis dose received and whether impairment was judged to be present. In total, 56 assessments were performed on the 15 participants at the various dose levels. In 7 cases on high dose and 3 cases on low dose impairment was judged to be present, but no cases on placebo. In assessments where a condition was judged to be due to a drug, 30 had received one of the three cannabis dose levels and only 2 were placebo conditions. On the basis of these observations, the general medical examination and standardised impairment testing applied by the FMEs were judged to be effective in determining both impairment and establishing condition due to a drug.

There was also a strong relation between the FMEs decision regarding the participant's impairment and the participant's subjective rating, which formed part of the mood questionnaire. These results are important for two reasons. First, they offer strong support for the validity of the FMEs decisions and for the effectiveness of the sobriety tests as detectors of impairment. Second, they offer further support for the view that, under the influence of cannabis, users are acutely aware of their impairment.

It is also interesting to note that, despite participants having smoked some form of cannabis before 42 of these examinations, on only 11 occasions did the FME consider the participant to be impaired. This finding could have implications for the number of cases that will be detected by the Field Impairment Testing recently launched in the UK by the police.

In addition to the general medical examination, pupil size was measured using a Pupillometer, supplied by Procyon Ltd. The Pupillometer showed a significant increase in pupil sizes 25-30 minutes after dosing. The difference was statistically significant for the placebo v high dose and the placebo v low dose. This suggests that this measure may be helpful in assessing if a person has recently smoked and may be impaired through cannabis, although this would require a baseline and an 'impaired condition' measure to be useful.

iv Driving response

The final key objective of the study was to consider the effects of cannabis on driving response. Statistically significant results which have been found for the simulator derived measures are given in the report. There was a reduction of average speed on the motorway when participants had the high or low doses of cannabis. This confirms the results from many previous studies. It strongly suggests that the participants as drivers are aware of their impairment, but attempt to compensate for their impairment by driving more cautiously. Participants did not know what strength of cannabis they had received, but knew there was a likelihood of having had something 'active' and so were perhaps being more careful. A post trial survey of participants showed that they were very good at guessing when they had taken the placebo dose and most participants even managed to correctly guess if they had the low dose or high dose.

In the simulator trials, participants reacted more slowly to a pulling-out event when they had taken the low dose of cannabis, suggesting a similar compensatory action for the effects of cannabis impairment. However, when taking the high dose this effect was not significant. This is probably due to the variability in the response data.

Similarly, there was no significant difference between braking reaction times. The mean response times increased slightly, but there was too much variability in the data for this to be statistically significant. This variability in the results when considering the impairing effects of cannabis has been observed by other researchers (Robbe & O'Hanlon, 1999). The variability of drug effects on individuals is well recognised and this seems to be even more in evidence with cannabis than with other drugs.

When considering the simulator tracking tasks, participants tended to drive less accurately on the left and right loops of the 'figure of eight' when they had been on the high cannabis dose. There was also a significant increase in their Standard Deviation of Lateral Position (SDLP) on the right loop when on the high dose as compared to the low dose of cannabis. This suggests that they were unable to control their steering as well when under the influence of the high cannabis dose. This again confirms previous observations that cannabis adversely affects drivers' tracking ability.

The mean time to move from stationary at a traffic light controlled junction once the lights had turned to red/amber on the driving simulator produced an interesting result. This was significantly reduced with high cannabis dose level, the reduction was in the order of ½ second between the placebo condition and high dose condition, and slightly less from the low dose to high dose. There are a number of possible explanations for this. It may suggest that in the 'observational' conditions of the driving simulator participants were aware of missing the traffic light change and so reacted slightly more quickly. Alternatively, the effects on the participants' internal clocks might have made them feel that they had been at the lights longer than they actually had and therefore heightened their attention to the imminent change in lights. It has been suggested (Riedel et al., 1998) that cannabis, in a similar way to alcohol at low doses, can have a stimulant effect on dopamine that may account for more risky behaviour in some circumstances. Other explanations are possible, however, and further assessment of this observation will be required.

The hazard perception[1] task did not produce any statistically significant results. Although reaction times were found to increase with dose level, there was too much variability in the data for statistical significance. An increase of 0.08 seconds between the placebo and low dose

[1] *The hazard perception task used in this research is quite different from the hazard perception tests being introduced for testing L-drivers*

and an increase of 0.14 seconds between the placebo and high dose was observed. This suggests that there may be an effect on the reaction time of participants responding to hazards, but it is quite a small effect which would require a much larger sample to determine whether or not it was statistically significant. This would also seem to confirm earlier observations of the effects of cannabis on the various aspects of driver performance; the effect on reaction time being somewhat indeterminant.

The mean tracking accuracy on the CTT test decreased with increasing level of dose. The placebo tracking accuracy was higher than either the high dose or resin tracking accuracy. Thus tracking accuracy does change with dose. The proportion of correct trials also decreased with increasing dose level. All participants were still quite accurate, but the difference from 99.5% accuracy when on placebo was statistically significantly different from the 97.0% accuracy when on the high dose. The HP and CTT results are of particular interest because the HP test was taken at least 75 minutes post smoking the cannabis, and the CTT test at least 85 minutes post dosing. Some of the acute impairment effects may well have diminished by then.

In summary, the results of this study show a broad consistency with the effects of cannabis on driver performance observed by previous researchers. In addition, the habits and attitudes of cannabis users in relation to driving have been explored for the first time in the UK.

Conclusions

The research has demonstrated the practicability of assessing the influence of cannabis on driving performance in a controlled clinical trials experimental situation. Participants were recruited, medically screened and tested under conditions of a strict protocol which had local ethics committee approval.

The maximum amounts of THC administered in the cannabis cigarettes were shown to be typical of that available with ‘street’ cannabis. Participants were generally able to distinguish between the effects of cannabis with active THC and placebo conditions. The subjective reports of smokers on the effects of smoking the various strengths of cannabis cigarettes showed an extremely good correlation between what participants thought they had smoked and the THC dosage in the cigarettes.

The feelings of the ‘highs’ experienced were also closely correlated with participants’ positive reactions as measured by a mood questionnaire. Given the controlled conditions of the experimental situation, the majority of participants also found the experience of smoking cannabis similar to their normal experience.

Previous studies have shown that simulated and actual driving and divided attention tasks which all require integrative mental processes are severely affected by alcohol. Simple attention / vigilance tasks are not so much affected and psycho-motor skills, especially tracking, and simple reaction time tasks are only affected at relatively high blood alcohol levels. Alcohol may, therefore, be seen as first disturbing higher cognitive processes, especially those that require integrative performances. Compared to those effects, the losses in psycho-motor skills and simple attentional processes are much smaller. In contrast, previous studies with cannabis show that it first seems to affect all tasks requiring psycho-motor skills and continuous attention. Thus, tracking tasks, which are very sensitive to short term changes in attention, are very sensitive to cannabis impairment. On the other hand, integration processes and higher cognitive functions are not as time critical. A short attention lapse can be compensated for by increased activity later.

In the case of the overall driving task, it seems that the negative effects of these short term distortions can be reduced by lowering the difficulty, and hence the time critical aspects, of the task. This would explain the frequently reported observation that drivers under the influence of cannabis drive at notably reduced speeds.

Results from the current study using the TRL driving simulator confirm the results from these previous studies. There was a reduction of average speed on simulated motorway driving when participants had the high or low doses of cannabis. This strongly suggests that the participants as drivers are aware of their impairment, but attempt to compensate for their impairment by driving more cautiously.

When considering the simulator tracking tasks, participants tended to drive less accurately on the left and right loops of the ‘figure of eight’ when they had been on the high cannabis dose. This suggests that they were unable to control their steering as well when under the influence of the high cannabis dose. This again confirms previous observations that cannabis adversely affects drivers tracking ability.

There is a variability in the results when considering the impairing effects of cannabis that has been observed by other researchers. The variability of drug effects on individuals is well recognised and this seems to be even more in evidence with cannabis than with other drugs. The failure to produce significant results on various driving performance measurements when compared to alcohol may be explained by the more variable effects of cannabis on participants.

The results of the driving related laboratory tests conducted in general did not produce statistically significant results. Although reaction times were found to increase with dose level, there was too much variability in the data for statistical significance. This suggests that there may be an effect on the reaction time of participants responding to hazards, but it is quite a small effect which would require a much larger sample to determine whether or not it was statistically significant. This again confirms earlier observations of the effects of cannabis on the various aspects of driver performance; the effect on reaction time being somewhat difficult to predict.

The general medical examination and standardised impairment testing applied by the FMEs were judged to be effective in determining both impairment and establishing condition due to a drug. Preliminary conclusions were drawn by the FMEs on the number and combination of impairment test failures which would allow a conclusion that the driver

was ‘impaired’. Further refinement and calibration of these techniques in the field, for use by both police officers and FMEs, is however desirable and is planned.

Overall, it is possible to conclude that cannabis has a measurable effect on psycho-motor performance, particularly tracking ability. Its effect on higher cognitive functions, for example divided attention tasks associated with driving, appear not to be as critical. Drivers under the influence of cannabis seem aware that they are impaired, and attempt to compensate for this impairment by reducing the difficulty of the driving task, for example by driving more slowly.

In terms of road safety, it cannot be concluded that driving under the influence of cannabis is not a hazard, as the effects on various aspects of driver performance are unpredictable. However, in comparison with alcohol, the severe effects of alcohol on the higher cognitive processes of driving are likely to make this more of a hazard, particularly at higher blood alcohol levels.

1 Introduction

Results from the study of the 'Incidence of alcohol and drugs in road accident fatalities' have consistently shown a large increase in the incidence of drugs in fatal road casualties (drivers, riders, passengers and pedestrians) since the last comparable study in the mid-1980s. The latest results show that among all road users illicit drugs were present in 18% of fatalities. These figures represent a six-fold increase in illicit drug taking when compared with the previous study (Everest, Tunbridge and Widdop, 1989). Cannabis constitutes around two thirds of the illegal drugs found.

Despite the increase in the incidence of drugs, it is not possible to say that drugs caused these deaths. There may be an association, but presence cannot be taken as evidence of causation - there is no way of telling how much was consumed and how long before the fatal accident. So far as cannabis is concerned, the prevalence in drivers was not significantly different from that of passengers, who can be taken as a (albeit imperfect) measure of the prevalence in the population as a whole. However, cannabis remains detectable in the body for up to four weeks after use - long after any impairment of driving.

In most surveys reported in Europe cannabis is the most frequently detected drug (de Gier, 1998). In a range of accident involved populations cannabis is found with an incidence between 2 and 12% with a mode incidence around 5-8%. This is certainly significantly above that of any other drug.

Previous research studies on cannabis and driving have focused largely on the effects of cannabinoids on driving performance. These studies have been almost exclusively experimental involving laboratory tasks, driving simulator and on road 'real driving' experiments. A much smaller number of studies have attempted to gain broader sociological information about driving habits under the influence of cannabis and what factors influence the decision to drive. The research reported here attempts to combine these two aspects, certainly for the first time in the UK, with a view to assessing the degree to which there may be a problem with cannabis in relation to driving.

Such international work as has been done suggests that, for up to two hours after a dose sufficient to give a 'high', there is impairment of the same order as alcohol at around the drink-drive limit (50–80mg/100ml) (Robbe, 1994).

Berghaus et al., (1995) performed a meta-analysis of the available data on the influence of cannabis (laboratory tests, driving simulator and real driving tests). A total of 324 experiments from 60 experimental studies are discussed. The authors classified the performance areas according to the sensitivity of THC-related impairment, based on the median (the concentration related to 50% of the cumulated results being significantly impaired). These plasma concentrations were not measured, but calculated based on the dose and pharmacokinetic parameters. On this basis, Berghaus equates the dose equivalent impairment of cannabis to be 11ng/ml in comparison to BAC of 73mg/100ml, however it should be noted this was the level 60 minutes after dosing, which is long after peak impairment.

It is well known that cannabis is often used in conjunction with alcohol. The few studies that have been conducted combining the effects of cannabis and alcohol on driving performance have tended to use relatively high doses of alcohol i.e. doses high enough to cause severe impairment alone. Anecdotal evidence suggests that regular cannabis users occasionally drink an amount of alcohol below the legal limit for safe driving, and then smoke cannabis before driving. It is therefore important to establish the degree of impairment caused by a low dose of alcohol in combination with cannabis.

In 1999 DETR commissioned a review (Ward & Dye, 1999) of the latest evidence of the impairment effects of cannabis. That report provided an overview of the effects of cannabis on driving and accident risk and identified areas where current knowledge was deemed to be insufficient to guide road safety policy. Those research questions have shaped and informed the current research project. The research project had the following objectives:

- To provide reliable data, under laboratory conditions, on the impairing effects of cannabis on driving.
- To determine the duration and extent of any impairment under different degrees of intoxication (using different levels of cannabis).
- To provide an overview of attitudes and habits of cannabis users in relation to driving and explore factors which may influence the decision to drive under its influence.

This report details the first phase of a research programme to examine the effects of cannabis, alone and in combination with alcohol, on psychomotor and cognitive skills relevant to car driving. The overall research aims to identify specific aspects of cognitive/ psychomotor behaviour that are affected by the two drugs, and to determine how individual differences might moderate the effects of the drugs on performance.

The first phase of work reported here addresses the effects of cannabis alone. This first trial took place in January and February 2000. A second phase study is planned to take place later in 2000 where the effects of alcohol and cannabis in a controlled trial combination will be studied.

2 Study design

2.1 Overview

Participants were asked to attend test sessions after consenting to the conditions outlined in an information sheet and having signed the consent form (see Appendix D), and completed a questionnaire that assessed their drug use and driving histories. Each participant was required to perform cognitive and psychomotor tasks under different conditions of drug dose. The tests were designed to assess vigilance, selectivity of attention, working memory, as well as speed and accuracy of decision-making in response to different stimuli.

Participants were medically screened by a doctor for suitability and also completed a questionnaire about their

cannabis smoking habits. Their identities were confidential during the trial and all identifying information was destroyed at the end of the trial.

Participants attended once for each treatment level, and had a week washout period between treatments. Blood, urine and saliva samples were taken on arrival and their breath alcohol level was checked to make sure that they had not been drinking. Participants then took a re-familiarisation drive on the simulator and a short simulator drive to provide a baseline measure. They smoked a cannabis cigarette under controlled conditions. They gave blood, and saliva samples 10 minutes after dosing started – this was the expected peak THC time and was expected to be highly correlated with subsequent impairment. They also gave a blood and saliva sample at 30 minutes after dosing started, which is when the impairment testing started. They drove the simulator for about 25 minutes during which time they were assessed on a variety of driving related measures. They also completed a compensatory tracking task (CTT) and a hazard perception task. The total testing time was just under 60 minutes (allowing for transfers between tests). During the test session they also completed a questionnaire with visual analogue scales at different times. This was to investigate their 'mood' and subjective effects being experienced. A final saliva sample was taken after testing.

Medical cover for taking and handling blood samples was provided and was available for resuscitation if necessary. A registered medical practitioner covered these medical aspects.

The trial used 4 treatment levels of cannabis, zero THC, Low THC, High THC which were National Institute on Drug Abuse (NIDA) supplied 'grass' based cannabis cigarettes and a resin based smoke using cannabis resin previously confiscated by Customs and Excise. Each participant was assigned to the three NIDA treatment conditions, in a fully randomised design; placebo THC, low THC dose (1.7% of active compound), high THC dose (2.6% of active compound) and for the final session prepared their own cigarette, using the Customs and Excise cannabis resin.

Each participant attended one test session for each treatment combination (at least one week apart), plus an initial screening interview. The test sessions were conducted from late afternoon until late evening, because most of the participants worked during the day, and also because this was a more natural time for them to be taking cannabis. Each test session was approximately two hours long. The results for the test session were recorded in a session case report form, see Appendix E.

2.2 Experimental design

The study was designed for a crossover design analysis of variance with planned comparisons. The design was a crossover for three treatment levels of NIDA supplied cannabis cigarettes, plus a fourth period where participants were supplied with cannabis resin and smoked it using their usual regime. The original design had planned that the fourth dosing with resin was randomised within the NIDA cigarette doses. However, the resin dose could not be 'blind' to the participant and so was treated separately.

The design is shown in Table 1. Fifteen participants were recruited for the trial with 5 allocated at random to each of the treatment groups. The design was fully balanced across the first three periods, but the fourth period was confounded with the resin dose.

Table 1 Experimental design

Group (5 participants per group)	*Period*			
	1	*2*	*3*	*4*
1	A	B	C	D
2	B	C	A	D
3	C	A	B	D

Dose levels:
A - placebo, B - medium dose,
C - high dose, D - dosing with supplied resin

2.3 Ethics committee

The experimental design and methodology were presented via a protocol document to the local area ethics committee. Ethics committee approval is required for any study that involves any risk to volunteer participants, however small the risk. The committee consists of registered medical practitioners with lay representation and meets once a month. The protocol submitted included a participant information sheet and an example of the participant consent form that was signed by all participants prior to being screened. The ethics committee approved the study but subject to certain conditions. These referred to details in the wording of the participant information sheet and the consent form. The ethics committee were also concerned about an idea that was originally proposed, that participants provide their own cannabis cigarettes for the final treatment session. This was in order to obtain an indication of what participants usually smoked, but was not viable because of the legal implications. In the event, cannabis resin was supplied under licence from Customs & Excise confiscated sources held at Heathrow, and participants were asked to use quantities similar to their normal use for the final period.

2.4 Sample size

The sample size was determined from data on impairment in earlier studies. Specifically, a similar study (Sexton, 1997) validated the use of a driving simulator for the detection of driver impairment through alcohol. This study used 18 participants and showed significant differences on some of the tasks. The power calculation, on a reaction time pulling-out event, suggested that 15 participants would show a statistically significant effect at the 95% confidence level on a 1-sided test with 84% power when comparing the difference in performance due to being impaired just below the legal alcohol limit. (In practice 2-sided tests were used for significance testing because it was not always clear in what direction cannabis changed the metric being evaluated). There were also pragmatic reasons for selecting this sample size because of the difficulty in locating and recruiting suitable participants within the time period available to conduct the first phase of this study.

2.5 Participants

Participants were males over 18 years of age who had a driving licence and used cannabis at least once per week. The sample was restricted to males because this avoided any possible complications that would have had to be considered in case females were already or became pregnant during the trial. It was thus more acceptable to the ethics committee. It may also be the situation that there are differences between males and females in terms of the effect on driving performance of smoking cannabis, due to physiological differences and/or driving style differences.

2.6 Recruiting

Participants were recruited through people who were known to the project team and who knew regular cannabis users. It was hoped that once potential participants had been contacted then they would know other cannabis users who also would be interested in helping with the trial. This recruiting technique is often referred to as a 'snowball' sampling approach.

Participants known to the 'link' people were invited to phone the project manager. The 'link' people were given a minimal amount of information about the trial, just the fact that male drivers who were regular cannabis users were required and that complete confidentially was assured. When participants phoned they were asked about their cannabis use, their availability and given some background information about the trial and the commitment being sought. If they were still interested they were asked to attend a screening session.

2.7 Screening

Participants were given a full medical screen to ensure that they were fit and healthy especially with respect to any respiratory problems, past or current. They attended a pre-booked session at TRL and were examined by a doctor. Prior to being examined they were asked to read a participant information sheet that informed them about the trial, and were asked to sign a consent form. An example of the screening document, which includes the participant information sheet and the consent form, is given as Appendix D. The inclusion/exclusion criteria are shown in Table 2.

2.7.1 Medical checks

The full range of medical checks is shown in the screening document (Appendix D). The participant was required to supply a urine sample which was checked to see that the participant had THC metabolites in his urine, and was thus a cannabis user. The urine sample was also used to check if the participant was a current polydrug user (i.e. a user of other drugs in addition to cannabis), which would have excluded him from the trial. Participants also supplied a blood sample for a blood chemistry check. Any participant who failed any of the screening checks was not included within the trial. This decision could not be made until the laboratory analysis of the blood and urine samples had been processed.

2.7.2 Questionnaire

A questionnaire regarding use of cannabis and other drugs had been developed by Kay Wright, a PhD student from University of Birmingham, who was closely involved with the trial. This questionnaire had been used to obtain a profile of the typical cannabis user and had been administered to a sample of 90 or so users. Participants who attended for screening were asked to complete this questionnaire, which was contained within the screening document (see Appendix D). The questionnaire provided a further method of checking the suitability of potential participants. A comparison of trial participants with other cannabis users is contained in Appendix A.

2.8 Analysis of samples

Samples of blood taken for screening purposes were processed by the pathology laboratory in Frimley Park Hospital, Surrey. These were delivered to the laboratories within hours of being taken and the results were usually available within 2-3 days.

Table 2 Inclusion and exclusion criteria

Criteria description	*Include if:*	*Exclude if:*
Gender	Male	Female
Age	≥18 and ≤ 60	<18 or >60
Car driver	For >12 months	<12 months
Cannabis user	For >12 months	<12 months
Cannabis frequency	At least weekly for 12 months	<weekly
History of substance abuse (not nicotine)	None	Any past
Medication	None	Any current
Respiratory disorder	None	Any history
Medical history	Normal	Any abnormalities
Height & weight	In normal range	Outside normal range*
Physical examination	In normal range	Outside normal range*
12 lead ECG	In normal range	Outside normal range*
Blood haematology and screening tests	In normal range	Outside normal range*
Visual acuity – via Snellen test	Acceptable	Unacceptable
Ability to commit to trial	Positive	Negative
Signed consent for trial	Prepared to give	Not given

* *There are established ranges defined for health purposes*

Samples of urine for screening and trial purposes were analysed by Epsom Hospital Laboratories Regional Assay Service. Samples of blood and saliva for the trial purposes were also analysed at Epsom. They were delivered to the laboratory on the evening of the trial using a TRL courier. The samples were kept in a cool box to control the temperature.

The urine sample results were available within 1-2 days. The blood and saliva sample results took several weeks to process. This is because the assaying of samples for relatively small quantities of cannabis metabolites is time consuming and will often require more than one analysis of the same sample in order to check the results.

3 Cannabis dose

Participants were given four different cannabis doses, one on each visit. The first three doses were pre-prepared 'grass' based cannabis cigarettes supplied by NIDA, each of a different strength. The fourth was prepared from cannabis resin. The resin was obtained under a Home Office licence from confiscated stock kept by Heathrow Airport Customs and Excise Department, which is usually used to train drug detection dogs.

3.1 Supply

The NIDA cigarettes were leaf/bud/florets mixed and rolled to a tightly controlled standard. They were stored frozen and with a humidity of about 10%. This needed to be increased to at least 14% prior to smoking in order to avoid a dry-smoke, which would not only be very harsh to participants but also would not convert the THC as required. Consequently, the cigarettes were humidified for 24 hours prior to smoking. The NIDA cigarettes weighed about 700 milligrams and were supplied in three strengths:

- Placebo containing about 0.005% ±0.002 of THC (active THC removed with a solvent).
- Low dose – 1.70% ±0.14 THC.
- High dose – 2.67% ±0.04 THC.

Three batches of cannabis resin each weighing 10grams were obtained under Home Office licence arrangements. These were assayed in order to determine the strength of the THC. The batch used by participants had about 1.7% of usable THC in total.

3.2 Control and licensing

Cannabis is an illegal drug and so a licence to hold and administer for the purposes of this research had to be obtained from the Home Office. A copy of the licence is shown in Appendix F. The control of the cannabis requires a drug book recording the supplier, quantities, when used etc. The imported cigarettes from NIDA were imported by The University of Birmingham under special licence conditions. The cigarettes were transferred to TRL and registered in the drugs control book. The Home Office issued a letter to DETR authorizing the supply of 30 grams of cannabis resin from Customs & Excise, Heathrow. A copy of the letter is shown in Appendix F. The use of the resin was controlled via the drugs book.

3.3 Administration

Cannabis cigarettes for the required period were removed from storage by the project manager and signed out from the drugs control book. (Only he knew the dose required, although a sealed envelope was available with the code-break). The cannabis cigarettes were placed in a humidifier that had been clearly marked with the participant identifying code. The cigarettes were humidified for 24 hours. Prior to smoking the cannabis cigarette was taken from the humidifier by the drug administrator, placed in a sealed tube and weighed to the nearest milligram. The tubes were then made available to the drug administrator who checked that the participant was given the correct cigarette to smoke. The original and residual weights of all NIDA cannabis cigarettes were recorded.

In the case of the resin-based cigarette this was prepared by the participant prior to the test session starting. (Similarly, those participants who preferred to use a pipe to smoke cannabis prepared the pipe before the test session commenced.). A quantity of resin was supplied to the participant which was weighed before and after each participant took what he wanted. The weight of resin used was thus determined and, knowing the strength of the resin from an assay analysis, enabled the maximum quantity of available THC to be calculated. An example of a participant preparing the resin with tobacco is shown in Figure 1.

Figure 1 Participant preparing resin for use with tobacco

The resin-based treatment was smoked in the participant's usual way, i.e. they could self-titrate. If participants wanted to stop smoking because they felt ill, or too 'high' or for any other valid reason then they were allowed to end the dosing session. This was noted on the case report form (Appendix E).

Determining the precise dosing of Δ^9-THC through

inhaled cannabis smoke is problematic. Previous studies have instructed participants to smoke cannabis cigarettes ad-lib (for example: Ohlsson et al., 1980, Lindgren et al., 1981, Cochetto et al., 1981, Cami et al., 1991, Perez-Reyes 1991, Robbe 1998). However, individual smoking techniques during ad-lib smoking vary to such an extent that differences in delivered Δ^9-THC to, and absorption from the lungs are inevitable. In order to control for inter- and intra-individual variations in smoking style, researchers have devised numerous standardised smoking procedures.

Typically, previous studies have standardised a combination of: i) draw-time/volume, ii) breathhold duration, iii) inter-draw interval time, and iv) number of draws (for example, Zancy and Chait 1988, Marks and MacAvoy 1989, Tashkin et al., 1991, Azorlosa et al., 1992). However, methodologies have been inconsistent in the number and timing of controlled variables.

3.4 Standardised smoking procedure

During sessions 1 to 3 of this study, participants smoked a single cigarette according to a standard smoking procedure (see Table 3). The paced smoking protocol was devised following a review of the relevant literature and a pilot study using placebo cigarettes.

Table 3 Standardised smoking protocol for sessions 1 to 3

Variable		Time
i	Draw-time	5 seconds
ii	Breathhold duration	5 seconds
iii	Inter-draw interval	30 seconds
iv	Number of draws	Various

Draw-time/draw volume

An increase in draw volume has been observed during ad-lib cannabis smoking, compared with tobacco smoking (Wu et al., 1988). The effects of increased draw volume on Δ^9-THC absorption, heart-rate and self-rated level of intoxication were measured in a study by Tashkin et al., (1991a), and no significant effects were found. However, it is important to standardize the inhalation volume of each draw in order to control for inter and intra-individual variation in smoking techniques. It is likely that standardizing draw-time may facilitate the control of draw-volume. However, differences in the volume of smoke drawn during each draw are also likely.

NIDA recommend that a 7-second draw is used. However, during the pilot run of the smoking procedure for this study, this was reduced to 5 seconds due to considerable discomfort experienced by the participants.

Breathhold duration

Assessments of ad-lib cannabis smoking have found breathhold durations between 7-25 seconds (Perez-Reyes 1982, Wu et al., 1988, Tashkin et al., 1991a, Block et al., 1997, Huestis et al., 1992). In a study by Tashkin et al., (1991a), prolonged breathhold time has been shown to enhance the absorption of Δ^9-THC from the lungs, potentiate the subjective feeling of intoxication, and increase heart-rate. However, in conjunction with a study by Zancy and Chait (1988), Tashkin et al., also found that extended breathhold (14 seconds) compared with a short breathhold (4 seconds) contributed to increased carboxyhaemoglobin boost and increased tar deposition. It is likely that a breathhold of 5 seconds would be sufficient for Δ^9-THC absorption, while reducing the detrimental effects of a more prolonged breathhold.

Inter-draw interval

The length of time between draws varies considerably during ad-lib cannabis smoking. Previous studies have reported inter-draw intervals in the range of 30-72 seconds (Zancy and Chait 1988, Tashkin et al., 1991b). Extended intervals are likely to promote losses of Δ^9-THC in side-stream smoke (Huestis et al., 1992), in addition to a decrease in the amount of cigarette smoked. During the pilot run, participants found 30 seconds to be comfortable.

Number of draws

It has been shown that the Δ^9-THC content of a cigarette is not differentially extracted from the plant material during the smoking procedure; i.e. similar amount of Δ^9-THC are present in both the unlit cigarette and the unsmoked portion (Huestis et al., 1992). Therefore, providing that the content of each cannabis cigarette is precisely the same, and that i), ii) and iii) in Table 3 are held constant, controlling the number of draws per cigarette is not likely to be necessary, providing the entire cigarette is consumed. However, the whole cigarette cannot be consumed since there will always be a butt remaining.

Table 4 shows the number of draws taken from each cigarette during the placebo, low and high Δ^9-THC dose conditions. The table also shows the maximum Δ^9-THC content available in each cigarette, which was estimated by weighing the portion that was not smoked. A verbal subjective report of how intoxicated each participant felt during each of the three sessions is included in the table.

Table 4 shows inter and intra-individual differences in the number of draws taken between sessions. These differences highlight the problem of controlling draw volume, where a decrease in draw volume results in an increase in number of draws. Two observations were made: i) in the majority of high Δ^9-THC dose conditions draw volume appeared to be reduced; i.e. participants tended to self-administer decreasing amounts of smoke during each draw. This behaviour is likely to be due to the high potency of the cigarette, and a reluctance to become too intoxicated. Participants in a study by Heishman et al., (1989) demonstrated similar smoking behaviour following a high Δ^9-THC dose condition (2.7%) compared to low (1.3%); ii) although humidified, each cigarette became unpleasantly harsh towards the end, resulting in shorter draw-times (2-3 seconds) and a greater number of draws.

Subjective reports on the effects of smoking

All subjective reports were consistent with the Δ^9-THC dose administered. During the placebo condition 6 participants felt a slight drug effect which wore off fairly

Table 4 Number of draws, maximum THC content (mg) and subjective reports of THC effects during 3 dose conditions, (P = Placebo, H = High, L = Low)

Subject	*Session*	*No.of draws*	*mg THC*	*Subjective report*
001	1 (H)	8	22.64	Considerably high, but had felt as high before.
	2 (P)	6	.03	A little high, but not much at all.
	3 (L)	7	11.53	A pleasant high, did not feel uncomfortable.
003	1 (P)	6	.03	The same hit as from a nicotine cigarette. Experienced a head rush that wore off immediately.
	2 (L)	8	11.61	A bit high, but nothing extreme.
	3 (H)	7	16.98	More high, but not too extreme – a happy feeling.
004	1 (L)*	8	11.66	Felt high.
	2 (H)*	7	16.77	Felt high, but more focused than week 1 – perhaps due to familiarity with environment.
	3 (P)	7	.03	Slight feeling of light-headedness which declined almost immediately.
006	1 (P)	6	.03	Unsure, but did not think they were stoned.
	2 (L)	6	10.38	Pleasant high, but had felt higher before.
	3 (H)	8	20.32	Considerable high immediately. Intense effects wore off before leaving the smoking room.
009	1 (P)	6	.03	Felt no effect.
	2 (L)	7	11.36	Good feeling close to usual high Intense feeling too soon.
	3 (H)	7	18.50	Would normally smoke that strength cigarette over half an hour. Neverexperienced such a feeling before.
010	1 (L)	6	9.81	Considerably more high than usual, but enjoyed the feeling.
	2 (H)	8	17.38	Similar feeling of high to normal, and enjoyable.
	3 (P)	7	.03	No effect.
011†	1 (L)	6	9.95	Felt the medium dose was administered.
	2 (H)	7	18.69	Felt the highest dose was administered.
	3 (P)	6	.03	A bit of a buzz.
014†	1 (L)	7	9.79	Felt the low dose was administered. Felt slightly high.
	2 (H)	8	17.01	Considerably high, but not an uncommon feeling.
	3 (P)	7	.03	Felt this was the placebo condition – felt no effect.
015†	1 (H)		18.96	Considerably high.
	2 (P)	6	.03	Felt this was the placebo condition – felt no effect.
	3 (L)	6	11.63	Felt slightly high.
023	1 (H)	6	18.24	Considerably high. Uncomfortable when smoking. A stronger feeling of intoxication than usually experienced.
	2 (P)	8	.03	Environment enhanced feelings No effect felt.
	3 (L)	7	10.46	Pleasant high close to usual experience.
030	1 (H)	9	16.82	Considerably high.
	2 (P)	7	.03	Pleasant feeling No effect felt Slightly high.
	3 (L)	10	10.64	Limit would smoke to if driving.
031	1 (L)	7	10.64	Slightly high. Not a pleasant experience, but felt in control Considerably high.
	2 (H)	6	18.05	Had felt this high before but did not enjoy the experience due to the clinical environment.
	3 (P)	6	.03	No effect felt.
032	1 (P)	7	.03	Mildly high, similar to a normal weak ‘joint’.
	2 (L)	8	11.80	Slightly high.
	3 (H)	9	20.16	Considerably high. Not an enjoyable experience.
033	1 (P)	6	.03	No effect felt.
	2 (H)	9	18.96	Considerably high for a while. Major effect wore off about half an hour later to a comfortable high.
	3 (L)	9	13.45	Slightly high. A relaxed feeling.

** Participant found it difficult to decide which week he felt most stoned*

† Participant was aware of the different drug conditions, and expressed his feelings in these terms

rapidly. Furthermore participant 011 was aware that a placebo condition was to be included, and yet experienced 'a bit of a buzz'. During the high Δ^9-THC dose condition the majority of participants (i.e.10) reported a strong drug effect, but felt that any unpleasantness was due to the clinical environment. A few found the effect too uncomfortable. Finally, reports following the low Δ^9-THC dose condition indicate that the majority of participants found the experience pleasant, and close to their usual state of intoxication. These subjective reports are consistent with the participant's assessment of their liking of the smoking effect as reported in section 5.2 and Appendix C from the mood questionnaire. Some commentators have criticised the use of NIDA supplied cannabis cigarettes in research of this type, on the basis that the cannabis used is of a low strength. Contrary to these reports the current research indicates that the NIDA supplied grass-based cannabis cigarettes were suitable for this trial using this smoking regime.

Ad-lib smoking

During the final session each participant was required to prepare and smoke a cannabis cigarette (or pipe) in his customary fashion. The cannabis was in the form of a solid block of cannabis resin obtained from Customs and Excise (UK). In the majority of cases, participants used a similar to usual amount of resin in each cigarette. However, participant 004 (3.58mg Δ^9-THC) stated that he had used less cannabis than usual because he would not normally smoke alone. Similarly, participant 032 (0.30mg Δ^9-THC) stated that he used less because he was concerned about becoming too intoxicated. Following smoking, participant 009 reported that he used less resin than he had thought (2.70mg Δ^9-THC), suggesting that the resin was not as strong as anticipated. Table 5 shows that a greater number of draws were taken during ad-lib smoking, compared with the paced smoking procedure. Furthermore, draw-time and breathhold duration was shorter in comparison.

Table 5 Ad-lib smoking compared with the standard smoking protocol

	Resin	*Placebo/Low/High THC dose conditions*
Mean number of draws	20.33 (range 13-34)	7.12 (range 6-9)
Mean draw-time	2.36 (range 2-3)	5 (all)
Mean breathhold duration	3.73 (range 2-7)	5 (all)

Controlling smoking technique variables is likely to reduce the problem of delivering a precise dose of Δ^9-THC. However, draw volume is difficult to control, and individual variation in the amount of smoke drawn during each draw, even when draw duration is timed, will ultimately affect Δ^9-THC absorption. Previous studies have shown that side-stream smoke losses, pyrolytic destruction, and inter-individual variation in Δ^9-THC absorption, distribution and metabolism also contribute to the problem of Δ^9-THC delivery (Robbe, 1994).

4 Measures

4.1 Overview

On arrival participants were checked for alcohol consumption using a Lion SD400 Breathalyser. They then answered various questions to confirm their eligibility and proceeded with the trial.

A diversity of measures was obtained during the trial. The case report form (see Appendix E), shows the measure and the time when it was obtained. First, participants were re-familiarized with the simulator, and this included a baseline measurement of how they drove round a 'figure of eight' course. The simulator was used later in the trial session to assess their reactions to other vehicles, how they drove round the 'figure of eight' and their response to a long delay at traffic light controlled junctions.

Participants were asked to complete a mood questionnaire at various stages of their trial session (Appendix E). They also underwent the sobriety tests that were administered by a Forensic Medical Examiner (FME). They were assessed on a video based hazard perception task and on a compensatory tracking task.

At different times during the experiment participants gave samples of urine, blood and saliva. The blood and saliva were to obtain a measure of how much Δ^9 -THC was in their system. The initial urine sample was checked using Dade-Behring poly-drug indicator strips that showed if the participant had recently been using cannabis, cocaine, amphetamines or opiates. The results from the indicator strip were cross-checked against the biochemistry laboratory analysis and proved to be very reliable.

4.2 Simulator

A range of measures was derived for each participant when driving the simulator and these are summarised in Table 6. The measures were designed to assess different skills. The motorway driving section was mainly trying to assess reaction times to adverse events, the 'figure of eight' measures control skills in staying within a lane on a road with changing radius curve, and the traffic light controlled junction provided a measure of vigilance while waiting for the light to change.

4.2.1 Description

The TRL Driving Simulator is a real medium-sized saloon car (a Rover 414Sli) surrounded by three 3 metre x 4 metre screens to the front providing 210° front/side image and one rear screen providing normal rear vision using vehicle mirrors.

The 'Virtual Reality world' is generated via the MultiGen 3-D modelling package and can be any driving scenario as required. Four projectors display the image on the screens; three linked to give continuous front/side image; a fourth at the rear of the car. The images are generated in 'real-time' and refreshed 60 times per second.

'State of the art' Silicon Graphics Reality engines generate the images. A further Silicon Graphics computer provides the Simulator operator station with an interface to the experiment. The operator has a 'birds-eye' view of the

Table 6 Simulated tasks and associated measures

Scenario	*Performance measure*
Motorway section with vehicles pulling out in front of the driven car.	Reaction times to pulling-out events, averaged over several events.
Motorway section with vehicles braking in front of the driven car.	Reaction times to braking events, averaged over several events.
Motorway section.	Minimum, maximum and average speed.
Following left hand non-circular curve of about 1 km radius.	Standard deviation of lane position from perfect path.
Following right hand non-circular curve of about 1 km radius.	Standard deviation of lane position from perfect path.
Dual carriageway with traffic lights, the lights are triggered to red so the driven vehicle has to stop and there is varying delay for green.	Response time to lights changing to red/amber and the time to crossing a point 10m from the stop line, averaged over several replications with varying time delays.

road layout and the position of all vehicles in the driving scenario, also a continuous representation of the use of the vehicle controls and speed.

The system generates intelligent vehicles, the behaviour of which can relate to that of the simulator vehicle or which behave as autonomous intelligent vehicles operating collision detection and avoidance with driving styles ranging from passive through 'normal' to aggressive.

The car bodyshell is mounted on hydraulic rams (in place of the shock absorbers) which supply motion to simulate the tilt and roll experienced in normal braking, acceleration and cornering. The car is equipped with speakers providing simulated engine, road tyre, and passing traffic noises. Video cameras are mounted in the car and participants' behaviour can be recorded during their drive. However, for this study no recordings were made because of the necessity of preserving the participants anonymity. An in-car intercom system enables the experimenter to give participants instructions.

This interactive simulator offers the advantages of providing a safe environment to study situations where the risks involved would be unacceptable in the real world. It provides control of conditions enabling repetition and reproducibility. This, combined with efficient data collection, is an ideal research tool. The TRL driving simulator has been shown to be a valuable tool for measuring drug-induced impairment in drivers (Sexton, 1997).

4.2.2 Motorway drive

A section of motorway was modelled based on the M3. It was about 16.7km in length and ended by turning in to a two-lane road that was modelled on the TRL small loop. The motorway consisted of 3-lanes with a hard shoulder. There were some gentle bends, slopes and bridges and it had the appearance of a normal motorway road, see Figure 2. Two versions were created with different traffic conditions.

One version was used for screening/familiarizing drivers and for their baseline drive. This consisted of traffic that behaved normally and created an impression of medium to light traffic flow. The traffic is generated by giving vehicles behaviours. If the behaviour is linked to the driven car then the traffic can be told to speed up or slow down relative to the driven car. In this way traffic speeds vary relative to that of the driven car and create an impression of far more vehicles on the road than there actually are. The simulation only needs to be concerned with what the driver sees, and hence traffic is only needed near the driven car.

Figure 2 An example of the simulated motorway scenario

The main version of the simulated motor traffic used a combination of vehicle behaviours. Some vehicles were programmed to slow down and speed up as in the screening/baseline version. Other vehicles were programmed to create a situation that the driver would have to react to, either by pulling out in front of the driver, or by braking for no apparent reason. The driver therefore had to modify his driving behaviour in some way, and the time taken to do this provided a measure of his response latency. A computer program was developed to automatically detect this driving behaviour change. The following order of conditions was investigated:

- Foot was on accelerator and has been removed.
- Foot was not on accelerator and the brake has been applied.
- A steering action has been made.

The driving speed was continuously recorded during the motorway drive. The minimum, maximum and average speeds were calculated over the whole motorway drive, excluding the first 1000 metres and last 1500 metres and any times when the driver stopped. The motorway section of the drive was about 16.7 Km in total length.

4.2.2.1 Pulling out events

Pulling out events are situations where a car pulls out in front of the driven car. The driver will normally have to

take avoiding action that can be detected and thus a reaction time can be estimated. Pulling out events were triggered when the trigger vehicle was 45 metres in front of the driven car. The exact circumstances varied from event to event since they were dependent on how the driver had been driving. The events were designed such that they could not be easily anticipated, but also such that the driver had time and space to respond. There were 5 such pulling out events on the motorway drive. The average of the 5 events was taken as a measure of the driver's reaction time.

4.2.2.2 Braking events

Braking events were controlled in a similar way to pulling out events, except that the trigger vehicle braked at a distance of 50m from the driven vehicle. Again, it was not intended to be easy to spot, nor to cause a crash. There were some situations where drivers did not take any detectable action. There were 3 braking events and the average of these was taken as a measure of the driver's reaction time.

4.2.3 Figure of eight

The 'figure of eight' loop is two 1-kilometer long loops with constantly changing radius. Participants were asked to drive between 30mph and 40mph and stay in the middle of the nearside lane. Because the curve is of a changing radius, drivers have to make almost continuous steering wheel corrections in order to stay in the centre of the road lane. The measure of success in the task was the standard deviation of their lateral position in the lane, the higher the standard deviation the more they had 'deviated' in the lane.

4.2.4 Traffic light controlled junction

The final stage of the simulator drive was a dual carriageway. There were four traffic light controlled junctions. The lights were pre-determined to be on red when the driver approached. The driver stopped and was kept waiting for a time varying between 15 and 25 seconds before the red/amber-green sequence started. Two measures of interest were analysed: the time to start from the onset of the red/amber light; and the time that it took to pass a point 10 metres into the junction. It was hypothesised that cannabis may affect drivers' responses to the changing lights. The average of the times from each junction was analysed.

4.3 Hazard perception[2]

Video films of different driving sequences were shown on a TV-screen. Participants were required to monitor continuously each scenario for hazardous situations. The assessment measures derived were the average reaction time to a number of hazardous situations (up to 5 per video film), and the proportion of potential hazards that were detected. Hazardous situations are those which would cause a driver to brake, steer or take some avoiding action, for example a dog running across the road. Potential hazards are situations which a driver would 'keep an eye on' because they could develop into a hazard, for example a child playing with a ball by the side of the road. Different video films were shown on each occasion the participant came for testing. The films were equivalent in terms of the mix of scenarios being shown and each lasted for about 12 minutes.

4.4 Compensatory tracking task

The participant manoeuvred a mouse cursor into continuous alignment with a moving target circle (Figure 3). Simultaneously the participant responded to white lights stimuli (2.5cm diameter) flashed at random intervals in one of the four corners of the screen. Responses to the peripheral stimuli were made by the participant clicking the mouse button. Failure to respond before the end of a 10 second trial (1 white light), or responding before a white light appears, was counted as an error. Reaction time (RT) was calculated by recording the mean response time in milliseconds to 72 white light stimuli over a 12 minute period (72 x 10 second trials) following a 3 minute practice trial (18 white lights).

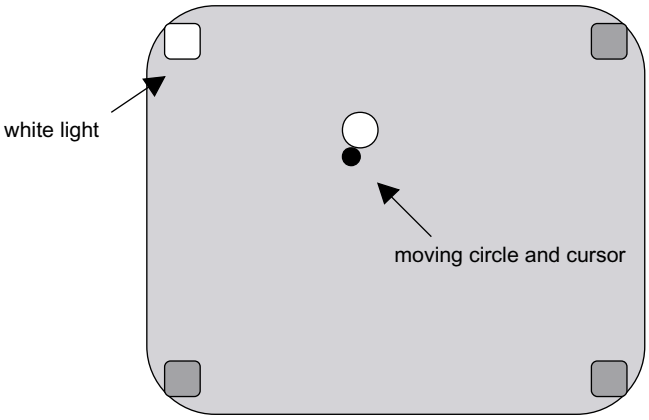

Figure 3 A diagramatic representation of the CTT test screen

This task required the participant to respond simultaneously in two ways. As such it is a divided attention task and so partially simulates the complex tasks required when driving. For each trial type mean accuracy and the standard deviation of accuracy were calculated as the mean deviation from the centre of the target circle. The mean and standard deviation of response times were computed as was the proportion of correct responses to the white light trials.

4.5 Mood questionnaire

Visual analogue scales (VAS) were used to assess mood state and physical symptoms. These were derived from a variety of sources: the 'Activation-deactivation checklist' (Richardson, 1995); the 'Physical symptoms scale' (Cohen, 1994); and the 'Marijuana scale' from Stephen Heishman at NIDA.

[2] *The hazard perception task used in this research is quite different from the hazard perception tests being introduced for testing L-drivers*

Participants placed a mark on a 100 mm line (see Appendix E) labelled with a mood state adjective (e.g. friendly, confident, muddled) from 'not at all' to 'entirely', or a physical symptom adjective (e.g. anxiety, dizziness, tiredness) from 'absent' to 'severe'. To ascertain their subjective physical responses to the cannabis dose they were receiving they placed a mark on a 100 mm line to statements such as: 'I have difficulty remembering'; and 'I notice that my heart is beating faster'.

In addition, an end of session questionnaire was presented requiring each participant to rate:

1 the strength of the overall drug effect on a 100 mm VAS from 'I felt no effect at all' to 'I felt a very strong effect';
2 their willingness to drive on a 100 mm VAS from 'I would not drive under any circumstances' to 'I would drive without any hesitation'; and
3 how much they liked the drug effect on a 100 mm VAS from 'disliked a lot' to 'liked a lot'.

4.6 Sobriety tests

The sobriety tests were conducted by an FME who was very familiar with the usual procedures followed for subjects in police custody. The FME used the standard sobriety test measures as recommended by Fleming & Stewart (1998). The test measures are shown in Table 7.

Table 7 Sobriety test list summary

General demeanour and behaviour	Conjunctivae?
State of clothing	Evidence of squint etc?
Speech: thick, slurred, over precise etc.	Any gross visual defect – are glasses used?
Condition of mouth	Pupil size
Pulse: rate and character	Pupillary reaction to
Temperature	– direct light stimulus
State of tongue	Horizontal gaze nystagmus
Breath	Vertical gaze nystagmus
Ears	Convergence
Heart	Walk and turn test
Blood pressure	One leg stand
Lungs	Finger nose test
Reflexes	Romberg test: internal clock
Eyelids red or swollen?	– 30 seconds estimates at
	Writing: copying from a text

The standardised examination form was taken from the Fleming & Stewart report and contains space to add remarks and conclusions. The impairment testing covered pupil size and reaction to light; presence of lateral and vertical nystagmus and convergence; walk and turn test; one leg stand; finger-nose test; and Romberg's test with internal clock. A full description of these tests can be found in Appendix B and a more detailed version of the sobriety test, as used in the trial, is shown in the case report form, Appendix E.. In addition, an example of handwriting was assessed. The physical examination included comments on the general demeanour and behaviour of the individual and examination of speech, pulse, temperature, ears, eyes, heart, lungs, blood pressure and reflexes.

Based on the participant's performance of these tests the FME concluded whether in her opinion the individual was impaired, and in addition whether there was a condition that might be due to the presence of a drug. This is in accordance with standard procedures.

The study was loaned a Pupillometer by Procyon. This is a device that takes a series of images of participant's pupils. It then calculates the average pupil size for each eye. An example of the pupil image is shown in Figure 4. Further details of the Pupillometer measurements can be found in Appendix B.

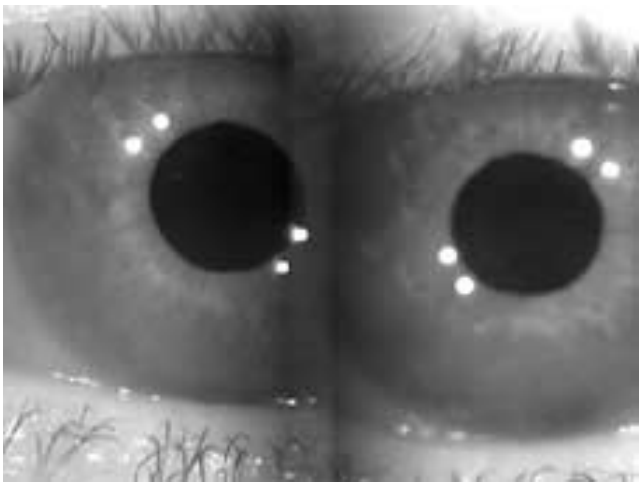

Figure 4 Image recorded by Pupilometer

4.7 Biochemistry

Participants gave samples of urine, blood and saliva prior to smoking cannabis. These were required to provide a baseline measure which facilitated checking for other drug use. Samples of blood and saliva were taken 10 minutes after smoking and 25-35 minutes after smoking. A final saliva sample was taken 95-100 minutes after smoking.

The saliva samples were collected by participants chewing a salivette for 5 minutes. This was centrifuged in order to extract the saliva. Two blood samples were taken at each sampling point to provide a backup sample. The blood samples were taken using a vacutainer. In order to reduce participant discomfort both arms were used to take the three blood samples.

The samples were dispatched to Epsom Hospital Laboratories Regional Assay Service on the evening of the sample being taken. The following substances were assayed in the analysis:

- Δ^8 THC - delta-8-tetrahydrocannabinol - a minor but psycho-active constituent of cannabis.
- Δ^9 THC - delta-9-tetrahydrocannabinol - the major psychoactive constituent of cannabis.
- THC-COOH - 9-carboxy-THC - the most rapidly produced metabolite, not psychoactive.
- CBD – Cannabidiol, the second main constituent of cannabis but not psychoactive, although it may interact with THC to produce effects.

The main sample of interest was the quantity of Δ^9 THC in blood and saliva, because this is the major psychoactive constituent of cannabis. Measures from both blood and saliva were required in order to investigate the relationship between them.

5 Analysis and results

The experimental design required 15 participants with 5 allocated at random to each dosing order group. In practice one person did not turn-up and was replaced. One other person attended the first session but was quite ill with flu for the following two weeks and decided not to continue. It was too late to replace him. The one replacement person did not smoke the resin because of missing the first week and the difficulty in extending the trial. Table 8 shows the sample of volunteers and the sample that was achieved, 34 potential participants were contacted and 15 were eligible, i.e. turned-up and met the criteria for inclusion. Of these, only 13 completed all the sessions with one dropping out (through flu) after the first visit.

Table 8 Number of volunteers screened, entered in the trial and sessions attended

	Number
Contacted for screening	34
Turned up for screening	24
Passed screening criteria	17
Failed screening criteria	7
Entered trial and completed 4 sessions	13
Entered trial and completed 3 sessions	14
Entered trial and completed 1 session	1
Entered trial and completed 0 sessions	1

The data from the case report forms was entered into an SPSS (Statistical Package for the Social Sciences) file. The data from the simulator was processed on the SGI (Silicon Graphics) computers and a file suitable for input to SPSS via Excel was generated. The average response times for pulling-in and braking events were based on just those events where a reaction could be determined.

The quantity of cigarette smoked, i.e. the number of milligrams consumed, multiplied by the strength of the THC gave a measure of the maximum dose of THC presented to the participant. The quantity of resin taken multiplied by the strength of resin gave an indication of the resin dose. The actual THC levels at peak dose (10 minutes after smoking) and peak impairment (30 minutes after dosing) were determined from the analysis of the blood and saliva samples.

The analysis took two approaches, first the treatment level was considered as a factor with 4 levels (placebo, low THC, high THC and resin). Secondly, the actual THC at peak impairment time was used as a continuous variable. The relationship between maximum dose presented and actual THC achieved was also investigated. The relationship between THC as measured by saliva and by blood at different times during the trial session was also analysed.

5.1 Statistical model

The study design was a crossover experiment where participants attended four trial sessions. At each session they smoked a different dose of cannabis. They smoked pre-prepared NIDA cannabis cigarettes on the first three visits, and these were of a different dose. The order of dosing was designed to be balanced such that the same number of participants took each dose level on each of the first three visits. Neither the participants nor the drug administrator knew what dose was being smoked, i.e. the administration was investigator blind. Participants always smoked cannabis resin on their fourth visit, the resin dose was thus fully confounded with the fourth visit effect. Participants obviously knew that they were smoking resin because they had to prepare the dose they wanted to smoke in the way they preferred.

The allocation of participant to order of dosing was random. The participant was treated as his own control. For most of the analyses, a hierarchic analysis of variance model was used with participant as the first level factor. The visit number (or period effect) was the next factor followed by the treatment factor (i.e. dose received). The analyses did not find any carry-over effects, and only two period effects were significant. Only the significant probability levels have been reported. Treatments were compared using designed contrasts as well as using the Tukey multiple range test option.

Two analyses were performed; one comparing the three NIDA supplied cannabis cigarette doses and one just comparing the resin dose with the placebo dose. The resin dose was confounded with any fourth period effect, but this was considered to be the best approach given that the resin dose could not be administered ‘blind’.

The analysis of the simulator, hazard perception and CTT measures used the SAS / GLM package module, (Statistical Analysis System / General Linear Model). The mood questionnaire had measures over time as well as between trial sessions and was analysed using SPSS.

5.2 Mood questionnaire

Factor analysis

A factor analysis was conducted on the mood checklist variables. Factor analysis is a statistical technique used to identify sets of variables which are measuring some underlying trait. It is used to reduce a number of correlated variables to a smaller set of factors. A three factor solution made logical sense and each factor was given a label, as shown in Table 9.

Table 9 Factors extracted from maximum likelihood factor analysis

Feelings/ signs of anxiety	*Feelings/ signs of listlessness*	*Feelings/ signs of wellbeing*
Increased heart rate	Dizziness	Clear
Shaking	Irritability	Alert
Bodily awareness	Sickness	Drowsy*
Palpitations	Difficulty concentrating	Calm
Anxiety	Slow	Cheerful
Loss of appetite	Tired	Difficulty remembering*
Sweating		
Tenseness		

**Variable coded in reverse direction*

A factor analysis was also conducted using maximum likelihood as the method of extraction, however with an oblique rotation. Three similar factors were extracted. The variables 'dry mouth' and 'confidence' did not correlate with the three factors in either of the analyses, and have been analysed separately.

The direction of the scale for the factors

A high score of anxiety reflects a high level of some or all of the following: increased heart rate, shaking, bodily awareness, palpitations, anxiety, loss of appetite, sweating and tenseness. It therefore indicates that the participant was experiencing strong feelings of anxiety. A high score of listlessness reflects a high level of dizziness, irritability, sickness, difficulty concentrating, slowness and tiredness. It therefore indicates that the participant was experiencing strong feelings of listlessness. A high score of wellbeing reflects a high level of feeling clear, alert, calm and cheerful, and a low level of feeling drowsy and having difficulty remembering. It therefore indicates that the participant was experiencing strong feelings of wellbeing and wakefulness.

Analysis and results

A repeated measure ANOVA (Analysis of Variance) and a one-way ANOVA were used to analyse the data. A range of post-hoc testing was carried out by assuming that participants in the different dosing conditions were different people. The SPSS package was used for the analysis. The results of all the mood questionnaire analyses are shown as Appendix C. In general, the results showed that with higher cannabis doses there was an increased level of anxiety and listlessness and a decrease in wellbeing. This was stronger just after dosing and decreased in effect as the effects wore-off. Participants reported a decrease in the drug effect over time, with the higher effects being associated with higher doses. They all reported a liking for the drug effect, but with higher doses were less willing to drive even 100 minutes after dosing.

5.3 Simulator tasks

The data from the simulator were pre-processed on the simulator computers in order to compute the reaction times on the motorway drive, to estimate the minimum, maximum and average speed on the motorway as well as calculate the standard deviation of the lateral lane position on the 'figure of eight'. The last simulator task was moving off from a traffic light controlled junction, and the computer calculated the time to move once the lights changed to red/amber. The time taken to cross a point 10m from the stop line was also calculated. The data were transferred to an Excel spreadsheet for input to SPSS and to SAS for statistical analysis.

5.3.1 Motorway drive

Table 10 shows the mean speeds while driving the motorway section. The speed data excludes the first 1000 metres and last 1500 metres and any parts of the drive where the participant had stopped. These speeds thus represent the typical speeds while driving.

Table 10 Minimum, maximum and average speeds on the motorway drive

Speed (mph)		*Sample size*	*Mean (mph)*	*Std. deviation*	*Std. error*	*95% Confidence interval for mean*	
						Lower bound	*Upper bound*
Minimum	Placebo	14	32.24	14.22	3.80	24.03	40.45
	Low	14	29.21	4.08	1.09	26.85	31.56
	High	15	26.76	7.57	1.95	22.57	30.95
	Resin	13	28.71	11.14	3.09	21.98	35.44
Maximum	Placebo	14	93.18	7.09	1.90	89.08	97.27
	Low	14	91.33	12.03	3.21	84.38	98.27
	High	15	91.79	7.40	1.91	87.69	95.89
	Resin	13	89.48	7.06	1.96	85.22	93.75
Average	Placebo	14	72.28	8.70	2.33	67.25	77.30
	Low	14	66.77	9.17	2.45	61.48	72.07
	High	15	66.70	8.34	2.15	62.08	71.32
	Resin	13	70.18	8.72	2.42	64.91	75.46

The analysis of variance showed that there were no significant differences between the minimum speeds driven under the different dose conditions. The mean minimum speed with the associated 95% confidence interval is illustrated in Figure 5.

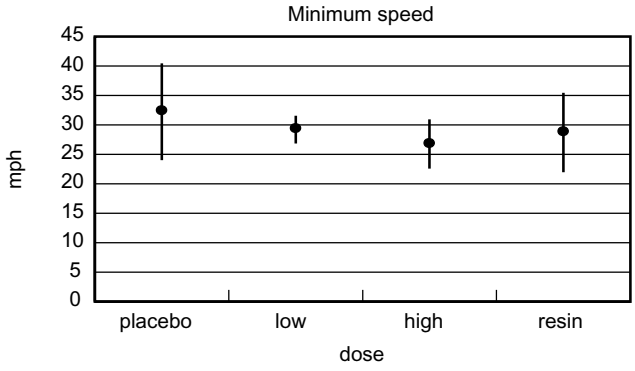

Figure 5 Minimum speed averaged for participants within each dose level

The analysis of variance showed that there were no significant differences between the maximum speeds driven under the different dose conditions. The mean maximum speed with the associated 95% confidence interval is illustrated in Figure 6.

The analysis of variance showed that there was a significant difference between the average speed driven when taking different levels of cannabis. The speed driven when taking the placebo was statistically significantly higher than the average speed when driving under the influence of either the high or low dose of cannabis. (Placebo v high: $F_{1,24}=7.12$, $p<0.05$, and placebo v low: $F_{1,24}=8.20$, $p<0.01$, i.e. the probability of the placebo having the same mean speed as the low dose is less than 0.01). The mean average speed with the associated 95% confidence interval is illustrated in Figure 7.

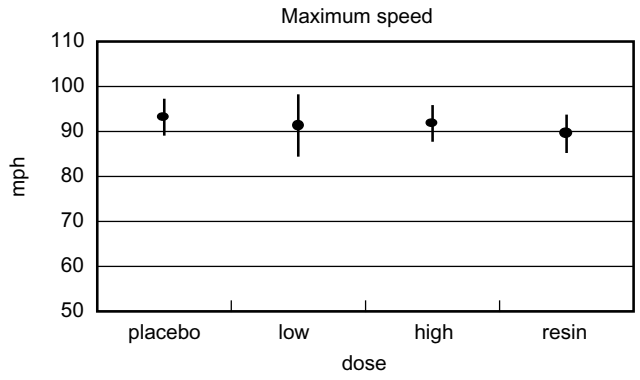

Figure 6 Maximum speed averaged for participants within each dose level

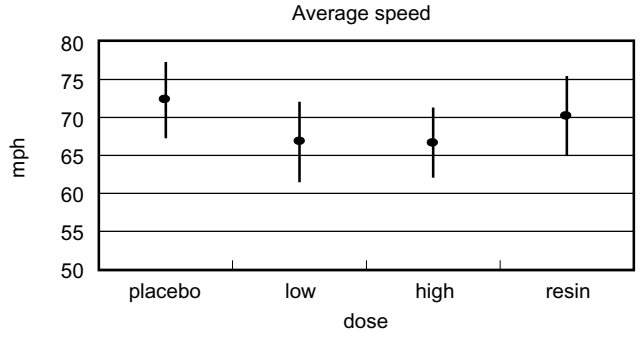

Figure 7 Average speed for participants within each dose level

The averaged minimum speeds suggest that, when impaired by cannabis, drivers do drive more slowly. This result was not statistically significant because of the variability in the data. However, the average speeds illustrate the same effect and was found to be statistically significant. Whilst there was no difference between the low and high dose levels, there was an average reduction of 6mph between the average speed on placebo and on the low and high dose levels. The average speed when smoking resin was 2mph lower than the placebo, but this was not sufficient to be statistically significant. It is, however, a shift in the same direction as seen on the low and high doses.

The reaction times to pulling-out and braking events are shown in Table 11. There is an average increase in reaction time when smoking the low cannabis dose, however this is not statistically significantly[3] different from the average reaction times under the other conditions.

Figure 8 shows the average reaction times to the pulling out events along with the 95% confidence intervals.

Figure 9 shows the average reaction times to the braking events along with the 95% confidence intervals. There are no statistically significant differences in reaction times, albeit the reactions for low cannabis dose look slightly longer. It might be expected that if there is a decrease in performance on the low cannabis dose then there would be more of an effect for the high dose. No such effect was found.

[3] *It is generally accepted that statistical significance is when there is only a 0.05 probability or less of accepting the null-hypothesis of no difference between the group means being compared.*

Table 11 Reaction times on the motorway drive

Reaction times (seconds)		*Sample size*	*Mean (secs)*	*Std. deviation*	*Std. error*	*95% Confidence interval for mean*	
						Lower bound	*Upper bound*
Pulling-out	Placebo	57	0.62	0.28	0.04	0.55	0.69
	Low	54	0.72	0.40	0.05	0.61	0.83
	High	58	0.67	0.31	0.04	0.59	0.76
	Resin	54	0.62	0.32	0.04	0.53	0.70
Braking	Placebo	34	0.70	0.34	0.06	0.58	0.81
	Low	33	0.84	0.43	0.07	0.69	0.99
	High	34	0.68	0.40	0.07	0.54	0.82
	Resin	28	0.71	0.30	0.06	0.59	0.82

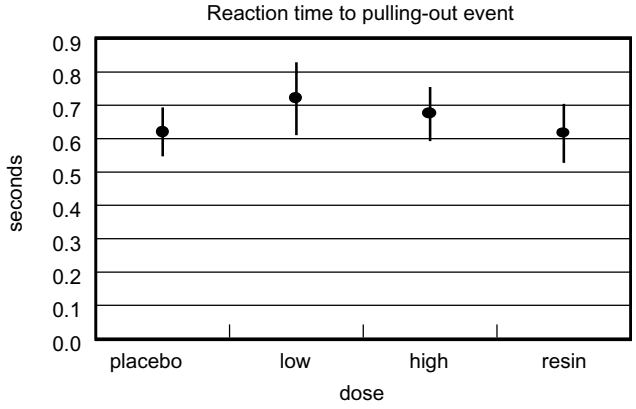

Figure 8 Reaction times to pulling-out events

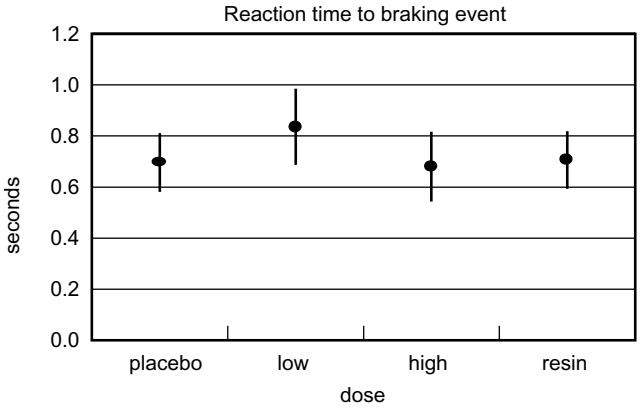

Figure 9 Reaction times to braking events

5.3.2 Figure of eight

The measure of interest when participants are driving round the 'figure of eight' was the SDLP (Standard Deviation of Lateral Position), in the road lane. This was measured by the variability in the lateral lane position and

the standard deviation of the lateral position was used as a metric. The mean values of the SDLP are given in Table 12. They show that as participants have higher doses of the cannabis there is more variation in their lateral position.

Table 12 Average standard deviation of lateral position on figure of eight drive

SD of deviation (metres)		*Sample size*	*Mean (metres)*	*Std. deviation*	*Std. Error*	*95% Confidence interval for mean* Lower bound	Upper bound
Left curve	Placebo	14	0.22	0.05	0.01	0.19	0.25
	Low	14	0.27	0.09	0.02	0.22	0.32
	High	15	0.30	0.12	0.03	0.24	0.37
	Resin	13	0.24	0.08	0.02	0.19	0.29
Right curve	Placebo	14	0.23	0.06	0.02	0.20	0.27
	Low	14	0.24	0.10	0.03	0.19	0.30
	High	15	0.31	0.15	0.04	0.23	0.40
	Resin	13	0.23	0.09	0.02	0.18	0.28

The analysis of variance showed that there is a statistically significant difference between placebo and high dose when on the left-handed curve of the 'figure of eight', ($F_{1,24}$=8.51, p<0.01). The difference between the placebo dose and the resin dose was not statistically significant, ($F_{1,12}$=4.02, p<0.10).

The analysis also showed that there is a statistically significant difference between placebo and high dose when on the right-handed curve of the 'figure of eight', ($F_{1,24}$=7.14, p<0.05), and a statistically significant difference between low dose and high dose, ($F_{1,24}$=5.24, p<0.05). The relationship between average SDLP and cannabis dose is shown in Figures 10 and 11.

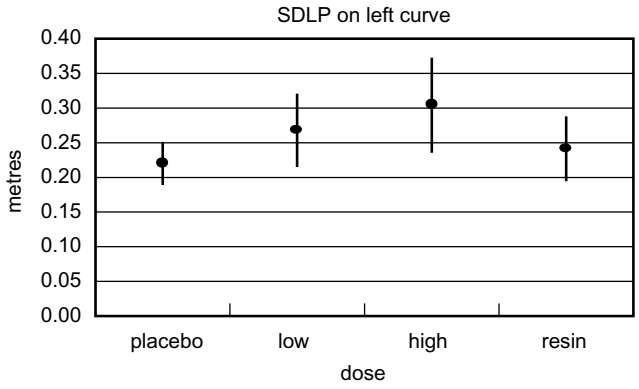

Figure 10 Average SDLP on left-hand curve

Figures 10 and 11 also show that there was far more variation between participants in their performance under the influence of the high dose of cannabis.

5.3.3 Traffic light controlled junction

The average time for the participant to move from the traffic light controlled junction when the lights went to red/amber, and the time to cross a point 10 metres after the junction stop line are shown in Table 13. The average time to respond decreased with dose, and was statistically significant when comparing the placebo with high dose ($F_{1,24}$=8.23, p<0.01) and low dose with high dose ($F_{1,24}$=6.37, p<0.02). The average time to the 10m point decreased with dose, but was not statistically significant when comparing the placebo with high dose ($F_{1,24}$=4.11, p<0.10) and low dose with high dose ($F_{1,24}$=3.70, p<0.10).

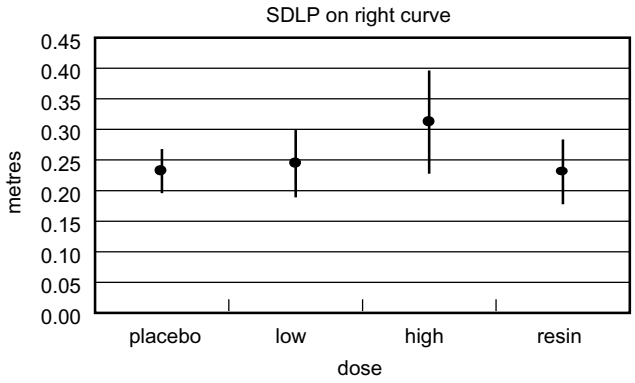

Figure 11 Average SDLP on right-hand curve

Table 13 Average time to cross 10m point after traffic lights change to amber

Time in seconds		*Sample size*	*Mean (secs)*	*Std. deviation*	*Std. error*	*95% Confidence interval for mean* Lower bound	Upper bound
To react to traffic lights	Placebo	14	2.81	0.59	0.17	2.45	3.17
	Low	14	2.71	0.62	0.17	2.37	3.08
	High	15	2.19	0.62	0.17	1.83	2.55
	Resin	13	2.69	0.62	0.19	2.29	3.09
To point 10m lights after traffic	Placebo	14	5.19	0.73	0.20	4.77	5.61
	Low	14	5.16	1.04	0.28	4.56	5.76
	High	15	4.65	0.94	0.24	4.12	5.17
	Resin	13	4.97	0.84	0.23	4.46	5.48

These figures suggest that on the high THC dose participants were responding more quickly to the stimulus of the lights changing. Participants took on average just 2.2 seconds to react to the traffic lights changing, which was ½ second less to react than when on the placebo dose. This result initially seems counter intuitive and merits further investigation.

5.3.4 Adjusting by placebo

An alternative approach to the analysis is to analyse the difference between a measure on the placebo dose with the measure when on other doses. This has the effect of controlling for the participant differences as well as giving a measure of the impact of the particular dose. The difference measure will include some small effect due to period, but overall this will be balanced across the sample. Table 14 shows the average adjusted mean differences for

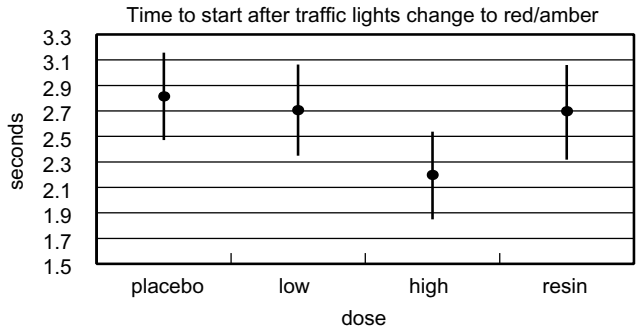

Figure 12 Average time for the participant to initiate moving from the traffic light controlled junction

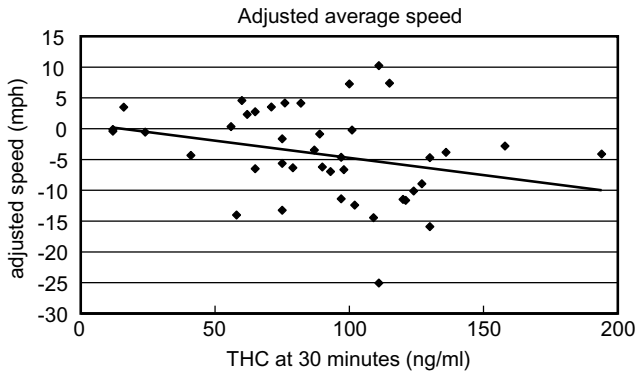

Figure 13 Adjusted mean motorway speed by cannabis dose 30 minutes after smoking

each of the simulator measures. The t-test has been used to check if the mean difference is significantly different from zero, i.e. is there a dose effect.

The significant results are very similar to those found in the previous analysis, (as they should be). However, what is interesting with this approach is being able to plot the adjusted measures by the Δ^9 THC levels at 30 minutes in order to show the net effect of the cannabis dose relative to placebo.

The relationship between the adjusted average motorway speed by Δ^9 THC levels is shown in Figure 13 and shows that, when on cannabis, participants generally drive slower, relative to how they drove when on the placebo. The higher the dose the slower they drive. The variation between participants increases with dose level but there is a clear trend, as indicated by the fitted line.

Figure 13 shows the individual speed change relative to the placebo dose for each participant. The x-axis is the THC level found in the blood sample 30 minutes after smoking. The figure shows a downward trend of adjusted speed with higher THC levels, suggesting that participants are reducing their speed with higher dose levels. However, there is considerable scatter in the data which makes interpretation difficult. This is facilitated if the data are grouped by treatment level, i.e. resin, low or high. Figure 14 shows the average speed on the motorway adjusted by

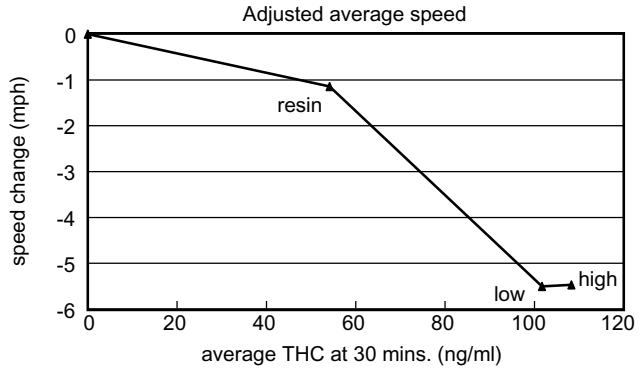

Figure 14 Adjusted average speed grouped within treatment level by Δ^9THC level

their respective placebo values and grouped within resin, low or high treatments. The figure now clearly shows the reduction in adjusted speed with increase in Δ^9 THC level at 30 minutes post smoking. The speed reduction for low and high doses of cannabis are very similar, but so are the THC levels in the blood after 30 minutes.

Similar graphs for reaction times to pulling-out and braking events on the motorway and for the SDLP measure while driving round the figure of eight are

Table 14 Mean values adjusted within participant by placebo

Dose		*Max. speed*	*Min. speed*	*Ave. speed*	*Pulling-out reaction*	*Braking reaction*	*Traffic light response*	*Left loop SDLP*	*Right loop SDLP*
Low	Mean	-1.85	-3.04	-5.50	0.212	0.116	-0.029	0.048	0.012
N=14	se	2.20	3.92	1.52	0.104	0.086	0.277	0.027	0.025
	t-test	-0.84	-0.78	-3.62	2.04	1.35	-0.11	1.78	0.49
	Prob*	ns	ns	<0.01	ns	ns	ns	ns	ns
High	Mean	-1.12	-5.13	-5.47	0.115	0.158	-0.639	0.082	0.081
N=14	se	2.17	4.85	2.49	0.082	0.173	0.261	0.027	0.037
	t-test	-0.52	-1.06	-2.20	1.40	0.91	-2.45	3.02	2.17
	Prob*	ns	ns	<0.05	ns	ns	<0.05	<0.02	<0.05
Resin	Mean	-3.05	-2.01	-1.14	0.046	0.019	-0.166	0.028	-0.003
n=13	se	1.96	3.17	1.71	0.045	0.060	0.272	0.014	0.019
	t-test	-1.56	-0.63	-0.67	1.02	0.31	-0.61	2.01	-0.14
	Prob*	ns	ns	ns	ns	ns	ns	ns	ns

**The probability of the mean not being significantly different from zero*

shown in Figure 15 and 16. These demonstrate the effect of increasing Δ^9 THC levels on placebo dose adjusted measures.

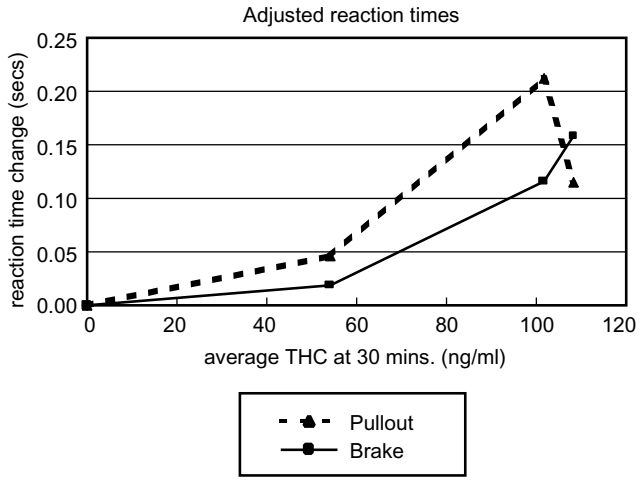

Figure 15 Adjusted reaction time grouped within treatment level by Δ^9THC level

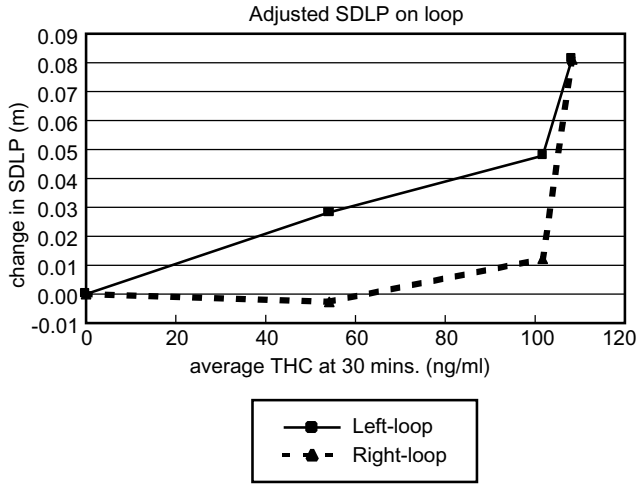

Figure 16 Adjusted SDLP grouped within treatment level by Δ^9THC level

5.4 Hazard perception

The hazard perception task measured the participant's reaction to a sudden hazardous event and whether the participant detected potential hazards. The average of valid reaction times and the proportion of hazards spotted were taken as measures. Table 15 shows the mean values for each of the different dose conditions.

The analysis of variance showed that there were no statistically significant differences between the means in each dose group. There is a strong suggestion from the data that the higher the dose the higher the reaction time, but there is too much 'noise' for this to be statistically significant. Figure 17 illustrates this result. There were no significant differences between the proportion of potential hazards that were 'spotted' and dose level.

Table 15 Hazard perception results by dose

						95% Confidence interval for mean	
		Sample size	*Mean*	*Std. deviation*	*Std. error*	*Lower bound*	*Upper bound*
Reaction time to actual hazards (seconds)	Placebo	14	1.42	0.37	0.10	1.21	1.64
	Low	14	1.50	0.36	0.10	1.29	1.71
	High	15	1.62	0.38	0.10	1.41	1.83
	Resin	13	1.38	0.46	0.13	1.10	1.65
Response to potential hazards (proportion spotted)	Placebo	14	0.200	0.192	0.051	0.089	0.311
	Low	14	0.100	0.188	0.050	-0.009	0.209
	High	15	0.240	0.314	0.081	0.066	0.414
	Resin	13	0.185	0.172	0.048	0.080	0.289

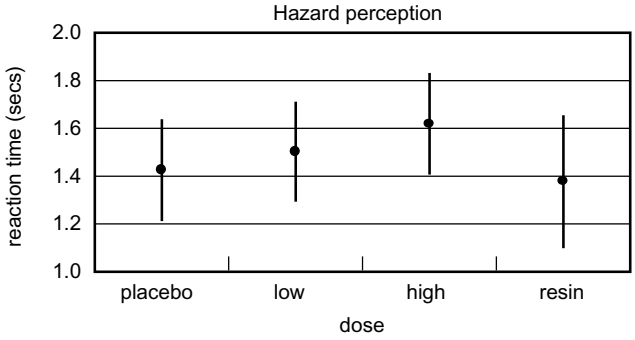

Figure 17 Hazard perception reaction time by dose

5.5 Compensatory tracking task

There were several measures derived in this task, the mean values are shown in Table 16. Only two of the measures that had statistically significant differences between dose mean values. These were: mean tracking accuracy, where the high dose mean was different from the placebo ($F_{1,24}$=5.27, $p<0.05$); and the proportion of correct responses, where the high dose mean was different from the placebo ($F_{1,18}$=5.84, $p<0.05$).

The mean tracking accuracy decreases as the THC dose increases, as does the proportion of correct responses to the 72 trials. This suggests that there is deterioration in performance due to the dose level of cannabis. This is illustrated in Figures 18 and 19 for the mean tracking accuracy and proportion correct respectively.

5.6 Sobriety tests

The sobriety tests were administered to participants by the Forensic Medical Examiner (FME) who then reached a conclusion about the impairment of the participant, and whether their condition was likely to be due to a drug. The decision reached was subjective, but one based on the results from the tests together with the FME's experience. Table 17 shows the decision reached. A Chi-squared test shows that there is a relationship between the rows and columns, i.e. the decision made does depend upon the dose

Table 16 Compensatory tracking task results by dose

		Sample size*	Mean	Std. deviation	Std. error	95% Confidence interval for mean: Lower bound	95% Confidence interval for mean: Upper bound
Mean tracking accuracy	Placebo	12	0.282	0.038	0.011	0.258	0.306
	Low	12	0.276	0.044	0.013	0.248	0.304
	High	11	0.262	0.031	0.009	0.241	0.282
	Resin	12	0.262	0.031	0.009	0.242	0.282
SE of tracking accuracy	Placebo	12	0.0046	0.0014	0.0004	0.0037	0.0055
	Low	12	0.0046	0.0015	0.0004	0.0037	0.0055
	High	11	0.0048	0.0016	0.0005	0.0037	0.0058
	Resin	12	0.0045	0.0020	0.0006	0.0032	0.0058
Mean response time (msecs)	Placebo	12	493.5	52.1	15.0	460.4	526.6
	Low	12	523.8	151.2	43.6	427.7	619.8
	High	11	502.8	94.8	28.6	439.1	566.5
	Resin	12	475.6	63.8	18.4	435.0	516.1
SE of response time	Placebo	12	15.51	3.96	1.14	12.99	18.02
	Low	12	25.35	30.63	8.84	5.89	44.81
	High	11	26.71	27.51	8.30	8.23	45.20
	Resin	12	17.54	16.15	4.66	7.28	27.80
Proportion correct trials	Placebo	12	0.995	0.012	0.004	0.988	1.000
	Low	12	0.984	0.019	0.005	0.972	0.996
	High	11	0.970	0.038	0.012	0.944	0.995
	Resin	12	0.992	0.013	0.004	0.984	1.000

* *Missing values are due to problems which occurred with the CTT equipment on a few occasions*

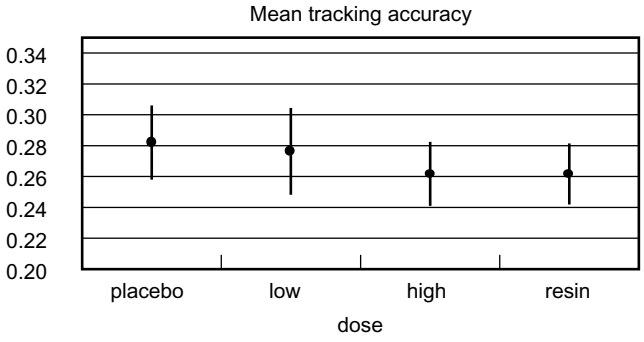

Figure 18 Mean tracking accuracy on CTT test

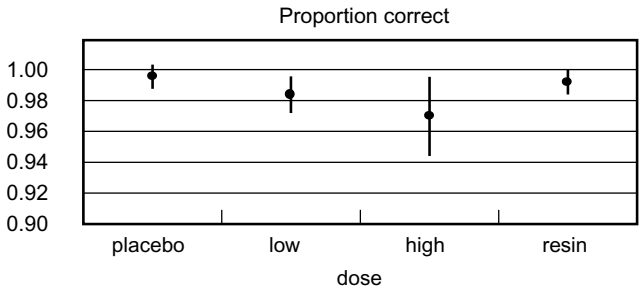

Figure 19 Proportion of correct trials on CTT test

Table 17 Decision on impairment

Dose		Impaired? Yes	Impaired? No	Total
Placebo	Count (row %)	0 (0%)	14 (100%)	14
Low	Count (row %)	3 (21%)	11 (79%)	14
High	Count (row %)	7 (47%)	8 (53%)	15
Resin	Count (row %)	1 (8%)	12 (92%)	13
Total	Count (Row %)	11 (20%)	45 (80%)	56

Chi-squared test = 11.6, df=3, p<0.01

received. This suggests that the sobriety tests are of value in deciding whether a participant is impaired. The table shows that with higher doses of cannabis the FME was more likely to decide that the individual was impaired.

Table 18 shows the decision reached and whether the condition was judged to be due to a drug. Again, a Chi-squared test shows that there is relationship between the rows and columns, i.e. the decision made does depend upon the dose received. This suggests that the tests have validity in helping the FME to decide whether a participant has a condition due to a drug. The table shows a good correlation with higher doses of cannabis.

Table 18 Condition due to a drug

Dose		Condition due to drug? Yes	Condition due to drug? No	Total
Placebo	Count (row %)	2 (14%)	12 (86%)	14
Low	Count (row %)	9 (64%)	5 (36%)	14
High	Count (row %)	12 (80%)	3 (20%)	15
Resin	Count (row %)	9 (69%)	4 (31%)	13
Total	Count (row %)	32 (57%)	24 (43%)	56

Chi-squared test = 14.8, df=3, p<0.01

The analysis of the sobriety tests showed that there is validation evidence in this test battery. A more complete report of this part of the trial can be found in Appendix B.

The measures obtained in the simulator were analysed to compare the performance of participants who were judged by the FME to be impaired with the performance of those judged not to be impaired. Tables 19 and 20 show the mean values for each measure for these two groups. The F-test tests the null-hypothesis that there is no difference between the two groups and has been adjusted for any participant effect. The results show that the decision as to whether the participant is impaired or not is confirmed across several of the simulator measures. In particular, there is a statistically significant difference between the groups on mean speed, and driving on the ‘figure of eight’ in both left and right-hand directions. For participants whose condition was judged to be due to a drug only the SDLP on the right-hand loop is statistically significant.

Table 19 Mean values for whether impaired or otherwise according to the sobriety test

Impaired		*Max. speed*	*Min. speed*	*Ave. speed*	*Pulling-out reaction*	*Braking reaction*	*Traffic light response*	*Left loop SDLP*	*Right loop SDLP*
Yes	Mean	92.3	30.1	66.2	0.75	0.79	4.64	0.32	0.34
	se	6.45	4.49	9.77	0.26	0.33	1.11	0.13	0.16
	Sample	11	11	11	11	11	11	11	11
No	Mean	91.3	29.0	69.6	0.65	0.71	5.07	0.24	0.24
	se	8.85	10.42	8.33	0.16	0.20	0.81	0.08	0.08
	Sample	45	45	45	45	42	45	45	45
	F-test	0.78	0.08	8.21	3.07	1.35	1.11	8.85	14.65
	Prob*	ns	ns	p<0.01	ns	Ns	ns	p<0.01	p<0.001

** The probability of the simulator measure mean values being the same*

Table 20 Mean values for whether their condition is due to a drug

Condition to drug		*Max. speed*	*Min. speed*	*Ave. speed*	*Pulling-out reaction*	*Braking reaction*	*Traffic light response*	*Left loop SDLP*	*Right loop SDLP*
Yes	Mean	93.3	28.7	68.8	0.67	0.75	5.02	0.27	0.27
	se	8.88	7.88	9.04	0.21	0.26	0.99	0.10	0.13
	Sample	32	32	32	32	31	32	32	32
No	Mean	89.1	29.8	69.0	0.67	0.69	3.94	0.24	0.23
	se	7.17	11.82	8.33	0.16	0.18	0.73	0.08	0.07
	Sample	24	24	24	24	22	24	24	24
	F-test	0.04	1.15	2.64	0.33	0.01	0.77	4.02	6.71
	Prob*	ns	ns	ns	ns	ns	ns	ns	p<0.05

** The probability of the simulator measure mean values being the same*

5.6.1 Comparison of subjective ratings and FME's decisions regarding impairment

As a further means of evaluating the effectiveness of the sobriety tests the FME's decisions regarding impairment were correlated with the participants' subjective ratings of impairment which formed part of the mood questionnaire. At 25 minutes post dosing participants were asked to rate how impaired they felt on a VAS of 1-100. These ratings were correlated with the FME's opinions. The correlation between sobriety decision and subjective rating of impairment at 25 mins = -0.48. The correlations are negative because the coding of the sobriety decision was 1=impaired, 2=not impaired, whereas the self assessment rating was 0 for not impaired to 100 for impaired (on the VAS 100mm scale).

This result is statistically significantly different from zero at the 95% level. The correlation is lower than would have been hoped but there is attenuation due to the fact that the sobriety decision is dichotomous and the maximum correlation value (in this instance) is about 0.70. Hence the 0.48 should be judged on a scale of -0.70 to 0.70 not the usual scale of -1.0 to 1.0.

Table 21 shows the mean self assessment ratings (1-100) of those subjects who were considered impaired compared with those who were considered not impaired.

Table 21 shows that there was a strong relation between the FME's decision regarding the participant's impairment and the participant's subjective rating. These results are important for two reasons. First, they offer strong support for the validity of the FME's decisions and for the effectiveness of the sobriety tests as detectors of impairment. Second, they offer further support for the view that, under the influence of cannabis, users are acutely aware of their impairment.

Table 21 Comparison between subjective ratings of impairment with FME's decision

	FME's decision	
Subjective ratings	*Impaired*	*Not impaired*
Impairment rating at 25 mins	53.9	26.2
Impairment rating overall	48.1	30.2
'Stoned' rating at 25 mins	66.5	40.7
'Stoned' rating overall	67.4	26.2

5.6.2 Pupillometer

Participants had their pupil size measured with the Procyon Pupillometer before dosing and 30 minutes after dosing. (The pupil size was also measured during sobriety testing using a reference card, see appendix B). The Pupillometer took 10 images of each pupil over a 2-second period and then calculated the average pupil size. Table 22 shows the mean difference between pupil sizes before and after dosing.

The analysis of variance indicated that there were statistically significant differences between placebo and high dose and between placebo and low dose. These were

Table 22 Increase in pupil sizes by dose

		Sample size	Mean difference in pupil size	Std. deviation	Std. error	95% Confidence interval for mean: Lower bound	95% Confidence interval for mean: Upper bound
Right eye (mm)	Placebo	14	0.041	0.268	0.072	-0.113	0.194
	Low	14	0.395	0.452	0.121	0.136	0.654
	High	14	0.240	0.287	0.077	0.076	0.404
	Resin	12	0.081	0.382	0.110	-0.156	0.318
Left eye (mm)	Placebo	14	-0.011	0.226	0.060	-0.141	0.118
	Low	14	0.394	0.482	0.129	0.118	0.671
	High	14	0.204	0.233	0.062	0.071	0.338
	Resin	12	-0.026	0.309	0.089	-0.217	0.165

significant for the right pupil (placebo v high:- $F_{1,23}$=5.49, p<0.05, and placebo v low:- $F_{1,23}$=12.0, p<0.01), and for the left pupil (placebo v high:- $F_{1,23}$=5.49, p<0.05, and placebo v low:- $F_{1,23}$=13.62, p<0.01). Figure 20 shows the mean differences for the right pupil and the 95% confidence intervals by dose.

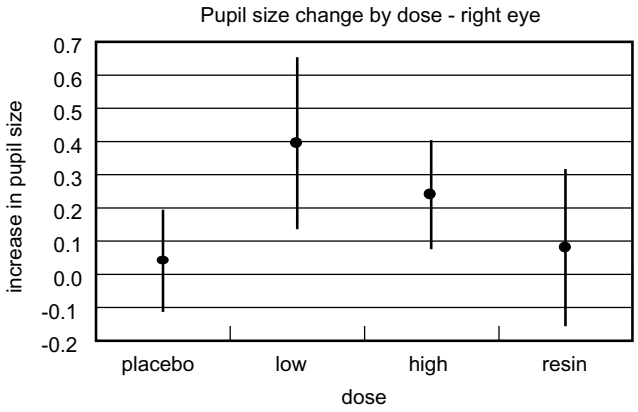

Figure 20 Mean differences in pupil size by dose

It is clear from Figure 20 that, whilst there is a difference in the mean pupil size when participants had received the low dose of cannabis, there is considerable variation between participants under both the low dose and under the influence of resin. Oddly, this effect was not apparent with the high dose of cannabis. It is also interesting to note that the effect is most pronounced with the low dose, and so appears not to be dose related.

Further discussion of the Pupillometer use and results can be found in the sobriety report – Appendix B.

5.7 Cannabis dose

Participants either smoked a pre-prepared NIDA cannabis cigarette or prepared a resin-based smoke in their usual way, i.e. pipe or mixed with tobacco. NIDA cigarettes were weighed before and after smoking, and so the weight smoked was known. An assay of the Δ^9THC content of the NIDA cigarettes was supplied from NIDA, hence the maximum dose can be calculated. We refer to the maximum dose because some THC will be lost in smoking and some absorbed by the remaining, unsmoked grass, (or tobacco in the case of resin). Figure 21 illustrates the maximum cannabis dose that could have been smoked in each condition.

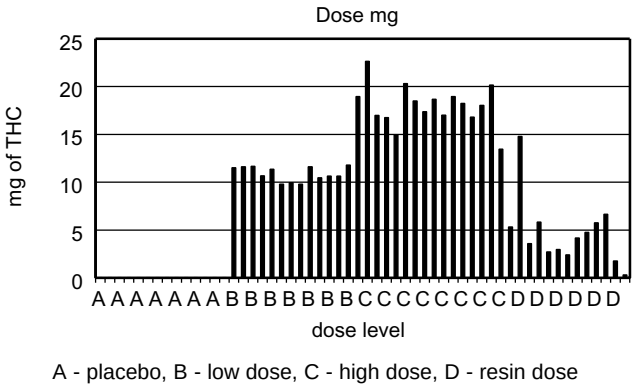

Figure 21 Maximum cannabis by dose level

It is clear that the placebo dose gave virtually no Δ^9 THC in the smoke. The maximum dose for low THC cannabis was on average about 11.5mg, for high THC it was about 18mg and for resin the maximum dose was about 4.7mg. One participant took a pipe full of resin and had a maximum THC level of nearly 15mg, which was as high as some participants on their high dose. However, the nature of smoking via a pipe makes it likely that an amount of this available THC would probably have been lost in side-stream smoke.

Figure 22 shows the average Δ^9 THC levels measured in the blood samples at 10 minutes and 30 minutes post dosing. Ten minutes post dosing has been suggested as the time when THC is at its peak, and Figure 22 shows that at this time the high THC dose produced the highest peak. Interestingly the THC levels after 30 minutes are very similar for the low and high treatment levels.

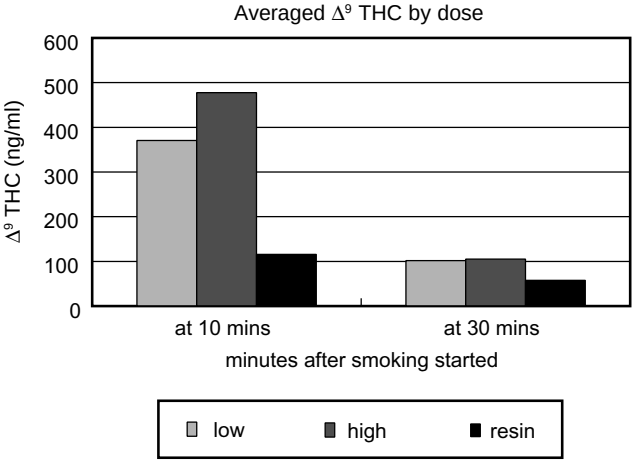

Figure 22 Average Δ^9THC levels by treatment level

Table 23 shows the maximum cannabis dose for each level of THC with the resultant Δ^9 THC levels 10 minutes and 30 minutes after smoking began. This clearly shows that the cannabis resin was much less potent than either of the NIDA doses. Figure 23 shows the ratio of maximum cannabis dose to body mass index, again at 10 and 30 minutes post dosing.

Table 23 Cannabis dose and blood Δ^9THC after 10 and 30 minutes

	Maximum cannabis dose smoked (mg)		*Δ^9 THC after 10 minutes (ng/ml)*		*Δ^9 THC after 30 minutes (ng/ml)*	
Dose	*Mean*	*SE*	*Mean*	*SE*	*Mean*	*SE*
Low dose	11.464	0.608	370.4	56.6	101.7	10.3
High dose	17.928	0.571	477.7	67.8	105.0	5.6
Resin	4.691	0.981	115.5	12.0	57.7	7.8

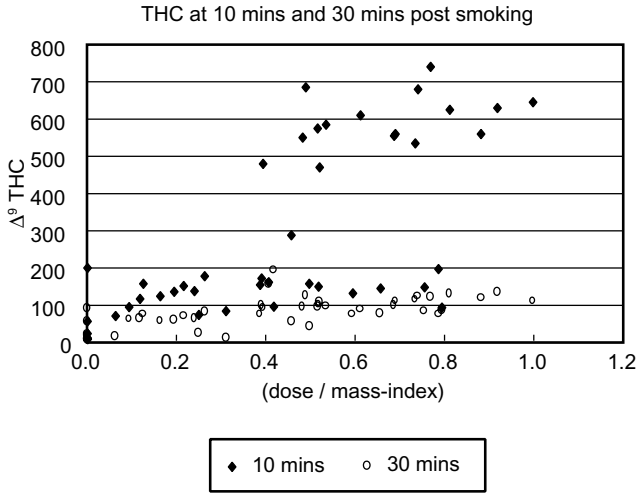

Figure 23 Cannabis dose / mass index v Δ^9THC after 10 and 30 minutes

An individual's body mass index is their mass in kg divided by their height in metres squared, i.e. a 75Kg person of height 1.8m has an index of 23.1. The ratio (dose/mass-index) is computed as the dose in ng/ml divided by the person's body mass index. The dose level is thus adjusted by the size and mass of the participant.

5.8 Blood v saliva

Analysis of the blood and saliva samples provided measures of the cannabinoids in the participant at 10 minutes and at 30 minutes post dosing. The main active compound is Δ^9 THC and this has been taken as the potentially impairing substance in the main analysis. The level of Δ^9 THC depends upon the dose given and the way the dose was smoked, i.e. if participants did not inhale or only took few small draws then they would not have received as large a dose as someone taking long draws and inhaling. This is unlikely because the smoking regime was closely monitored and controlled by the drug administrator, who observed and recorded the smoking style of each individual.

The relationship between maximum dose as a ratio of body mass index and subsequent blood THC level at 30 minutes, as in Figure 23, suggests a relationship between dose and achieved THC levels, but there is also a lot of 'noise' in the data. This is probably due to variations in smoking style and possibly the participant's metabolism.

Figure 24 shows the relationship between THC in saliva and THC in blood 30 minutes after smoking commenced. It does not show any particularly strong relationship. The two very high saliva values are probably due to oral contamination from the cannabis cigarette. This can be caused by bits of leaf getting into the mouth and contaminating the saliva.

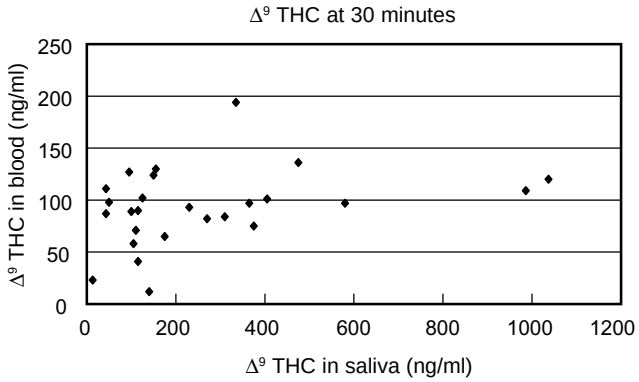

Figure 24 Cannabis Δ^9THC at 30 minutes for saliva and blood

6 Summary of main results and discussion

6.1 Summary of main results

The results of statistical analyses of the observations on driving performance tasks and driving related laboratory tests are summarized in Tables 24 and 25. Table 24 shows the statistically significant results for the simulator derived measures. There was a reduction in average speed on the motorway when participants had the high or low doses of cannabis. This confirms the results from many previous studies. It strongly suggests that the participants, as drivers, are aware of their impairment, but attempt to compensate for this impairment by driving more cautiously. Participants did not know what strength of cannabis they had received, but knew there was a likelihood of having had something 'active' and so were perhaps being more careful. A post trial survey of participants showed that they were very good at guessing when they had taken the placebo dose and most participants even managed to correctly guess if they had the low dose or high dose.

Anecdotally, a quotation from an older regular cannabis user may be relevant:

'The stuff makes you drive too slow and if there's one thing old people don't need it's something that makes them drive slower than they already do. I don't mean slow to a point where you endanger others, but just five or ten mph under the limit and that happens

because you figure you're already racing along at a nice clip and are surprised when you look at the speedometer and see you're not'

(Keliher, 1997, p. 80,).

Table 24 Summary of significant results for simulator measures

	Placebo v low dose	*Placebo v high dose*	*High v low dose*	*Placebo v resin dose*
Maximum speed on m'way	NS*	NS	NS	NS
Minimum speed on m'way	NS	NS	NS	NS
Average speed on m'way	<0.01	<0.05	NS	NS
Reaction time to pulling-out events	NS	NS	NS	NS
Reaction time to braking events	NS	NS	NS	NS
SDLP on left loop	NS	<0.01	NS	NS
SDLP on right loop	NS	<0.05	<0.05	NS
Time to react from traffic lights	NS	<0.01	<0.02	NS

* *Only probabilities less than 5% have been reported, i.e. NS means that the probability of rejecting the null-hypothesis is greater than 0.05, i.e. there is at least a 5% chance that there is no difference between the two dose levels being compared.*

Table 25 Summary of probability of significant results for other measures

	Placebo v low dose	*Placebo v high dose*	*High v low dose*	*Placebo v resin dose*
Hazard perception reaction time	NS*	NS	NS	NS
Hazard perception spotting potential hazard	NS	NS	NS	NS
CTT mean tracking accuracy	NS	<0.05	NS	<0.05
CTT standard error of tracking accuracy	NS	NS	NS	NS
CTT response time	NS	NS	NS	NS
CTT standard error of response time	NS	NS	NS	NS
CTT proportion of correct trials	NS	<0.05	NS	NS
Change in pupil size from Pupillometer (left eye)	<0.01	<0.05	NS	NS
Change in pupil size from Pupillometer (right eye)	<0.01	<0.05	NS	NS

* *NS is as defined for Table 24*

In the simulator trials, participants reacted more slowly to a pulling-out event when they had taken the low dose of cannabis, suggesting a similar compensatory action for the effects of cannabis impairment. However, when taking the high dose this effect was not significant. This is probably due to the variability in the response data, although the mean response time for the high dose group was half way between the low dose and the placebo. Clearly, if response time was dose related we would have expected the high dose to produce a slower reaction time than the low dose.

Similarly, there was no significant difference between the braking reaction times. The mean response times increased, but there was too much variability in the data for this to be statistically significant. This variability in the results when considering the impairing effects of cannabis has been observed by other researchers (Robbe & O'Hanlon, 1999). The variability of drug effects on individuals is well recognised and this seems to be even more in evidence with cannabis than with other drugs. The expected statistical power of the double blind crossover trial methods used here was based on previous work on alcohol (Sexton, 1997). The failure to produce significant results on measurement when compared to alcohol may be explained by the more variable effects of cannabis on participants.

When considering the simulator tracking tasks, participants tended to drive less accurately on the left and right loops of the 'figure of eight' when they had been on the high cannabis dose. There was also a significant increase in their Standard Deviation of lateral position (SDLP) on the right loop when on the high dose as compared to the low dose of cannabis. This suggests that they were unable to control their steering as well when under the influence of the high cannabis dose. This again confirms previous observations that cannabis adversely affects drivers' tracking ability.

The mean time to move from stationary at a traffic light controlled junction once the lights had turned to red/amber on the driving simulator produced an interesting result. This was significantly reduced under the influence of the high cannabis dose, the reduction was of the order of ½ second between the placebo condition and high dose condition, and slightly less between the low and high doses.

There are a number of possible explanations for this. It may suggest that in the 'observational' conditions of the driving simulator participants were aware of missing the traffic light change and so reacted slightly more quickly. The effects on the participants' internal clock might make them feel that they had been at the lights longer than they actually had and therefore are more prepared to move off.

Alternatively, it has been suggested (Riedel et al., 1998) that cannabis, in a similar way to alcohol at low doses, can have a stimulant effect on dopamine that may account for more risky behaviour in some circumstances. Other explanations are possible, however, and further assessment of this observation will be required.

The results of the driving related laboratory tests conducted in this study are given in Table 25. The hazard perception task did not produce any statistically significant results. Although hazard perception reaction times were found to increase with dose level, there was too much variability in the data for statistical significance. An increase of 0.08 seconds between the placebo and low dose and an increase of 0.14 seconds between the placebo and high dose was observed.

This suggests that there may be an effect on the reaction time of participants responding to hazards, but it is quite a small effect which would require a much larger sample to determine whether or not it was statistically significant. This would also seem to confirm earlier observations of the effects of cannabis on the various aspects of driver performance; the effect on reaction time being somewhat indeterminant.

The mean tracking accuracy on the CTT test decreased with increasing level of dose. Tracking was more accurate under the placebo condition than under either the high dose or resin. However, there was no significant difference between placebo and low dose, so it is not possible to say conclusively that tracking accuracy changes with dose.

The proportion of correct trials also decreased with increasing dose level. All participants were still quite accurate, but the difference from 99.5% accuracy when on placebo was statistically significantly different from the 97.0% accuracy when on the high dose. The HP and CTT results are of particular interest because the HP test was taken at least 75 minutes post smoking the cannabis, and the CTT test at least 85 minutes post dosing, by which time some of the acute impairment effects may well have diminished.

The Pupillometer showed a significant increase in pupil sizes 25-30 minutes after dosing. The difference was statistically significant for the placebo v high dose and the placebo v low dose. This suggests that this measure may be helpful in assessing if a person has recently smoked and may be impaired through cannabis, although this would require a baseline and an 'impaired condition' measure to be useful.

In summary, the results of this study show a broad consistency with the effects of cannabis on driver performance observed by previous researchers. In addition, the habits and attitudes of cannabis users in relation to driving has been explored for the first time in the UK.

6.2 Discussion of results

In reviewing the results of this research it is important to consider previous studies, particularly in relation to four key issues identified in the review by Ward & Dye (1999). These were exposure, biological response, acute psychomotor response and driving response.

i Exposure

Care was taken to ensure that, as far as possible, participants were experienced cannabis users, (defined as using cannabis at least once a week for the past 12 months or more). Conformity with this criterion was checked by testing participant's urine samples during medical screening. Failure to screen out novice users had produced problems for previous experimenters (Robbe & O'Hanlon, 1999) with participants being incapable of performing tests on higher doses.

Although legal and ethical considerations restricted the availability of cannabis samples it was important to establish that the samples we used would be capable of producing the physiological effects experienced by users in normal smoking sessions. A recent survey of cannabis sold in Dutch coffee shops (Niessink, 2000) showed average non-Dutch marihuana (smokable cannabis leaves) to contain about 5% THC. A review of the availability of herbal cannabis varieties in the UK (Atha, 2000) showed a similar average, with a range between 1 and 8%. Both the higher dose and lower doses used in our experiments were within this range.

Prior to this research, few studies have attempted to gain broader sociological information about driving under the influence of cannabis. A comparison between the participants in the current study and a group of regular cannabis users in the West Midlands (Appendix A) showed the trial group to be fairly typical. Both groups showed a reluctance to drive after consuming more than 4 units of alcohol, believing their driving to be significantly impaired. The majority of both groups thought that cannabis impaired their driving, but only to a slight degree.

A recent study of recreational drug use associated with driving in Scotland (Ingram et al., 2000) surveyed a representative population aged 17-39. Of these, 4% admitted driving under the influence of cannabis in the past 12 months. Of the 39 drivers who admitted taking cannabis 10 thought it improved their driving and the majority of the rest thought it had no effect.

ii Biological response

In considering the results of the present study, the biological response of the participants to the consumption of cannabis is of fundamental importance. Blood and saliva measurements were taken immediately prior to dosing and at 10 and 30 minutes post dosing. This early measurement of THC level is particularly important as it has been shown that plasma THC peaks very quickly (around 7 minutes) irrespective of potency, with peak physiological effects (e.g. heart rate and subjective impairment levels) being reached approximately 10-15 minutes later. Many previous experiments which did not measure THC levels until at least 30 minutes post-dosing are likely to have missed this peak and thus recorded significantly lower THC levels, which fall off very rapidly. (Perez-Reyes, 1999).

Several recent papers have sought to correlate plasma THC levels with general impairing effects of cannabis and the specific effects on psycho-motor skills related to driving performance. (Berghaus et al., 1995; Kruger & Berghaus, 1995). The latter paper reviews the available literature to compare the effects of different concentrations of alcohol and THC on various aspects of driving performance. The authors deduced an equi-potency of effects which related a BAC of 73mg/100ml to a plasma concentration of 11ng/ml THC. However, such concentrations relate to the THC levels 60 minutes after smoking a typical cigarette containing 10 mg of THC. In addition, the levels of THC used in the analysis were in the main not based on measured blood values, but were predicted values calculated from the THC concentrations in the cigarettes and time of testing as obtained from a pharmaco-kinetic model derived by Sticht (1995). There is still considerable debate as to the absolute levels derived from such models and Huestis (1999) gives higher plasma THC values comparable to our own measurements.

It is clear that relating absolute levels of THC in blood to either subjective impairment effects or psycho-motor effects on driving is complex. Ideally, there is a need to take several values over time, but this has rarely been done in assessments on driving skill.

Even in situations where the plasma THC is measured directly, rather than estimated, it is necessary to take into account the smoking habits and cannabis consumption of those being tested. Whereas, as stated earlier, it is essential to exclude novice cannabis users from experimental trials, other studies (e.g. Agurell et al, 1984) using radioactively labelled THC have shown that in heavy consumption (say

of 50–100mg THC per day) the background level of THC can exceed that of freshly smoked THC by up to a factor of 10, for up to a week after smoking the labelled cannabis. This needs to be borne in mind in considering any threshold level of THC which might be seen as relating THC level to impairment which may affect driving at a given time after smoking (Sticht, 1995).

It is also important to make any assessment of the impairing effects of cannabis relatively soon after dosing as the acute effects of cannabis intoxication are known to wear off quite quickly, certainly within 2 hours.

The subjective reports given in Table 4 of the effects of smoking the various strengths of cannabis cigarettes showed an extremely good correlation between what participants thought they had smoked and the THC dosage in the cigarettes. The maximum amounts of THC administered were around 10mg for the low dose and 20mg for the high and the majority of participants were able to distinguish between the effects of these doses and placebo. The subjective feelings of the 'highs' experienced were also closely correlated with the participants' 'liking' of the smoking effect as stated in the mood questionnaire. Making allowance for the experimental situation, the majority of participants also found the experience of smoking cannabis similar to their normal experience.

iii Acute psychomotor response and tests of impairment

It is of the utmost importance to try to relate the observations derived from this experimental study to the situations likely to be encountered in real life drug driving cases. Part of the experimental procedures therefore included the formal sobriety testing of participants. Two experienced FMEs examined the participants and carried out a comprehensive physical examination to see whether the suggested standard 'impairment' tests currently used were effective in detecting impairment due to cannabis.

In a 'real life' case of suspected drug driving a police officer may arrest a person if he has reasonable grounds to suspect that the person has been driving or attempting to drive whilst unfit through drugs; (Section 4 (1) of the Road Traffic Act 1988 as amended by the Road Traffic Act 1991 (RTA)). In this context being unfit is defined in section 4(5) of the Road Traffic Act 1988 '*…a person shall be taken to be unfit to drive if his ability to drive properly is for the time being impaired*.'

At the police station following such an arrest a FME will be called to examine the person. The aim of this examination is twofold. First, to ensure that the person is fit to be in a police station, that there is no evidence of injury (e.g. head injury following a road traffic accident) or a medical condition (e.g. hypoglycaemia) requiring urgent treatment. Second, to determine whether the driver is impaired to drive or whether there is a condition that might be due to a drug. In order for the police to require a specimen (blood or urine) for analysis (Section 7 (3) (c) RTA) the FME needs to advise the police officer that the condition of the person required to provide the specimen might be due to a drug.

There has been controversy as to whether the FME had to certify impairment before the police could lawfully request a blood sample for analysis. Case law has now clarified this issue so that police can lawfully request a blood sample for analysis even if the person is not demonstrably impaired at the time of the FME's examination.

Furthermore, the Crown Prosecution Service has recently issued guidance on the relevant question 'might a suspect's condition be due to some drug?' The FME's advice to the police officer can be based upon conclusions drawn not only from his or her own examination of the suspect but also from relevant information gleaned from the suspect or the police concerning earlier events. However, exactly what constitutes a 'condition due to a drug' remains an issue for debate.

Even if in practical circumstances, demonstration of impairment is not required it is clearly desirable to be able to distinguish between cases where impairment is judged to be present and where the condition is due to a drug. In normal circumstances all those judged to be impaired will also be judged to have a condition.

The results of the sobriety testing clearly show a strong correlation between cannabis dose received and whether impairment was judged to be present. In total, 56 assessments were performed on the 15 participants at the various dose levels. In 7 cases on the high dose and 3 cases on the low dose the participant was judged to be impaired. In none of the cases where a participant had received the placebo was he judged to be impaired. In assessments where a condition was judged to be due to a drug 30 had received one of the three cannabis dose levels and only 2 were placebo conditions.

On the basis of these observations, the general medical examination and standardised impairment testing applied by the FME were judged to be effective in determining both impairment and establishing condition due to a drug. Further refinement and calibration of these techniques in the field is however desirable and is planned. (Tunbridge et al., 2000).

It is also interesting to note that, despite participants having smoked some form of cannabis before 42 of these examinations, on only 11 occasions did the FME consider the participant to be impaired. This finding could have implications for the number of cases that will be detected by the Field Impairment Testing recently launched in the UK by the police.

iv Driving response

The results of this study with respect to the final key issue relate to the effects of cannabis on driving response. Kruger & Berghaus (1995) reviewed the available literature to compare the effects of various concentrations of alcohol and THC on various aspects of driving performance. They looked at eight classifications of driver performance from 197 studies involving alcohol and 60 involving cannabis. The eight driver performance measures covered in these studies include all those commonly used in the assessment of alcohol and drugs on driver performance. These tasks were: simulated/real driving; coding/decoding information; divided attention; visual function; tracking ability; psychomotor tasks; reaction time and attention/vigilance.

This meta-analysis of studies shows that actual driving, coding and divided attention tasks, which all require integrative mental processes, are severely affected by alcohol. Simple attention/vigilance tasks are not so much affected and psycho-motor skills, especially tracking, and simple reaction time tasks are only affected at relatively high blood alcohol levels. Thus, the effect of alcohol may be seen as first disturbing higher cognitive processes, especially those that require integrative performances. Compared to those effects, the losses in psycho-motor skills and simple attentional processes are much smaller.

In contrast, cannabis first seems to affect tasks requiring psycho-motor skills and continuous attention. Thus, tracking as a fast feedback loop between continuous visual inspection and spontaneous motor reaction to changes is very sensitive to short term distortions in attention. On the other hand, integration processes and higher cognitive functions are not as time critical as motor reactions. A short attention lapse can be compensated for by increased activity afterwards.

In the case of the integrative task of driving, the negative effects of these short term distortions can be reduced by lowering the difficulty, and hence the time critical aspects, of the task. This would explain the often reported observation that drivers under the influence of cannabis drive at notably reduced speeds.

7 Conclusions

This research has demonstrated the practicability of assessing the influence of cannabis on driving performance in a controlled clinical trials experimental situation. Participants were recruited, medically screened and tested under conditions of a strict protocol which had local ethics committee approval.

The maximum amounts of THC administered in the cannabis cigarettes were shown to be typical of that available with ‘street’ cannabis. Participants were generally able to distinguish between the effects of cannabis with active THC and placebo conditions. The subjective reports of smokers on the effects of smoking the various strengths of cannabis cigarettes showed an extremely good correlation between what participants thought they had smoked and the THC dosage in the cigarettes.

The feelings of the ‘highs’ experienced were also closely correlated with the participant’s positive reactions to a mood questionnaire. Given the controlled conditions of the experimental situation, the majority of participants also found the experience of smoking cannabis similar to their normal experience.

Previous studies have shown that simulated and actual driving and divided attention tasks which all require integrative mental processes are severely affected by alcohol. Simple attention / vigilance tasks are not so much affected and psycho-motor skills, especially tracking, and simple reaction time tasks are only affected at relatively high blood alcohol levels. Alcohol may, therefore, be seen as first disturbing higher cognitive processes, especially those that require integrative performances. Compared to those effects, the losses in psycho-motor skills and simple attentional processes are much smaller

In contrast, previous studies with cannabis show that it first seems to affect all tasks requiring psycho-motor skills and continuous attention. Thus, tracking tasks, which are very sensitive to short term changes in attention, are very sensitive to cannabis impairment. On the other hand, integration processes and higher cognitive functions are not as time critical. A short attention lapse can be compensated for by increased activity later.

In the case of the overall driving task, it seems that the negative effects of these short term distortions can be reduced by lowering the difficulty, and hence the time critical aspects, of the task. This would explain the frequently reported observation that drivers under the influence of cannabis drive at notably reduced speeds.

Results from the current study using the TRL driving simulator confirm the results from these previous studies. There was a reduction of average speed on simulated motorway driving when participants had the high or low doses of cannabis. This strongly suggests that the participants as drivers are aware of their impairment, but attempt to compensate for their impairment by driving more cautiously.

Also in the simulator trials, participants reacted more slowly to a pulling-out event when they had taken the low dose of cannabis, suggesting a similar compensatory action for the effects of cannabis impairment. However, when taking the high dose this effect was not significant.

When considering the simulator tracking tasks, participants tended to drive less accurately on the left and right loops of the ‘figure of eight’ when they had been on the high cannabis dose. This suggests that they were unable to control their steering as well when under the influence of the high cannabis dose. This again confirms previous observations that cannabis adversely affects drivers tracking ability.

There is a variability in the results when considering the impairing effects of cannabis that has been observed by other researchers. The variability of drug effects on individuals is well recognised and this seems to be even more in evidence with cannabis than other with drugs. The failure to produce significant results on various driving performance measurements when compared to alcohol may be explained by the more variable effects of cannabis on participants.

The results of the driving related laboratory tests conducted in general did not produce statistically significant results. Although reaction times were found to increase with dose level, there was too much variability in the data for statistical significance. This suggests that there may be an effect on the reaction time of participants responding to hazards, but it is quite a small effect which would require a much larger sample to determine whether or not it was statistically significant.

This again confirms earlier observations of the effects of cannabis on the various aspects of driver performance; the effect on reaction time being somewhat difficult to predict.

It is of paramount importance to try to relate the observations derived from this experimental study to the

situations likely to be encountered in real life drug driving cases. The development of drug driving policy is heavily reliant on the ability of police officers to detect impairment due to drugs at the roadside. This then needs to be properly followed up at a police station with a full assessment of the driver's condition being made by a police surgeon. An evidential, blood or urine sample might then be requested and a case of suspected drug driving considered for prosecution.

The experimental procedures therefore included the formal sobriety testing of participants, carried out by two experienced Police Surgeons/Forensic Medical Examiners. The results of this sobriety testing clearly show a strong correlation between cannabis dose received and whether impairment was judged to be present.

On the basis of these observations, the general medical examination and standardised impairment testing applied by the police surgeons were judged to be effective in determining both impairment and establishing condition due to a drug. Preliminary conclusions were drawn by the police surgeons on the number and combination of impairment test failures which would allow a conclusion that the driver was 'impaired'. Further refinement and calibration of these techniques in the field, for use by both police officers and police surgeons, is however desirable and is planned.

Overall, it is possible to conclude that cannabis has a measurable effect on psycho-motor performance, particularly tracking ability. Its effect on higher cognitive functions, for example divided attention tasks associated with driving, appear not to be as critical. Drivers under the influence of cannabis seem to compensate to some extent for the impairment, that they recognise, by reducing the difficulty of the driving task; e.g. by driving more slowly.

In terms of road safety, it cannot be concluded that driving under the influence is not a hazard, as the effects on various aspects of driver performance are unpredictable. In comparison with alcohol however, the severe effects of alcohol on the higher cognitive processes of driving are likely to make this more of a hazard, particularly at higher blood alcohol levels.

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9 References

Agurell S, Gillespie H, Halldin M, Hollister L E, Johansson J, Lindgren J E, Ohlsson A Szirmal M and Wildman M (1984). *A review of recent studies on the pharmacokinetics and metabolism of D9-tetrahydrocannabinol, cannabidiol and cannabinol in man; in Marihuana 84*. Proceedings of the Oxford Symposium on Cannabis. Oxford, Washington DC: IRL Press.

Atha M (2000). *Types of cannabis available in the UK*. Independent Drug Monitoring Unit, Wigan

Azorlosa, J L, Heishman S J, Stitzer M L and Mahaffey J M (1992). *Marijuana smoking: effect of varying D9-tetraydocannabinol content on number of puffs*. Journal of Pharmacology and Experimental Therapeutics 261: 114-122

Belgrave B E, Bird K D, Chesher G B, Jackson D M, Lubbe K E, Starmer G A and Teo R K C (1979). *The effect of (-) trans-D9-tetrahydrocannabinol, alone and in combination with ethanol, on human performance*. Psychopharmacology 62: 53-60.

Berghaus G, Scheer N and Schmidt P (1995). *Effects of cannabis on psychomotor skills and driving performance – a meta-analysis of experimental studies*. Proceedings of 13th International Conference on Alcohol, Drugs and Traffic Safety – T95. Adelaide, NHMRC Road Accident Research Unit. University of Adelaide, pp. 403-409.

Bird K D, Boleyn T, Chesher G B, Jackson D M, Starmer G A and Teo R K C (1980). *Intercannabinoid and cannabinoid-ethanol interactions and their effects on human performance*. Psychopharmacology 71:181-188.

Block R I, Erwin W J, Farinpour R and Braverman K (1997). *Sedative, stimulant, and other subjective effects of marijuana: relationship to smoking technique.* Pharmacology, Biochemistry and Behaviour 59(2) 405-412

Brookoff D, Cook C S, Williams C and Mann C S (1994). *Testing reckless drivers for cocaine and marijuana*. The New England Journal of Medicine 331: 518-522.

Cami J, Guerra D, Ugena B, Segura J and Dela Torre R (1991). *Effect of subject expectancy on the THC intoxication of disposition from smoked hashish cigarettes*. Pharmacology, Biochemistry and Behaviour 40: 115-119

Chait L D and Perry J L (1994). *Acute and residual effects of alcohol and marijuana, alone and in combination, on mood and performance*. Psychopharmacology 115: 340-349.

Chesher G B, Franks H M, Hensley V R, Hensley W J, Jackson D M, Starmer G A and Teo R K C (1976). *The interaction of ethanol and Δ^9-tetrahydrocannabinol in man. Effects on perceptual, cognitive and motor functions*. The Medical Journal of Australia 2: 159-163.

Chiang C N and Barnett G (1984). *Marijuana effect and delta-9-tetrahydrocannabinol plasma level*. Clin. Pharmacol. Ther. 36: 234-238.

Cimbura G, Lucas D M, Bennett R C and Donelson A C (1990). *Incidence and toxicological aspects of cannabis and ethanol detected in 1394 fatally injured drivers and pedestrians in Ontario (1982-1984)*. Journal of Forensic Sciences 35: 1035-1041.

Cochetto D M, Owens S M, Perez-Reyes M, DiGuiseppi S and Miller L L (1981). *Relationship between plasma delta-9-tetrahydrocannabinol concentration and pharmacologic effects in man*. Psychopharmacology 75: 158-164

Cohen C, Pickworth W B, Bunker E B and Henningfield J E (1994). *Physical symptoms scale*. Pharmacology, Biochemistry and Behaviour 47: 919-926

de Gier J J (1998). *Road traffic and illicit drugs Review of investigations of prevalence of illicit drugs in road traffic in different European countries*. P-PG/Circrout (98) 1. Strasbourg, Council of Europe, Pompidou Group.

Everest J T, Tunbridge R J and Widdop B (1989). The incidence of drugs in road accident fatalities. Research Report RR202. TRL Limited, Crowthorne.

Fleming P and Stewart D (1998). *Drugs and driving: training implications for police officers and police surgeons*. Police Research Group. Home Office, London.

Harder S and Rietbrock S (1997). *Concentration-effect relationship of Δ^9-tetra-hydrocannabiol and prediction of psychotropic effects after smoking marijuana*. Int. J of Clin. Pharm. Ther. 35: 155-159.

Heishman S J, Arasteh K and Stitzer M L (1997). *Comparative effects of alcohol and marijuana on mood, memory and performance*. Pharmacology Biochemistry and Behavior 58: 93-101.

Heishman S J, Stitzer M L and Bigelow G E (1989). *Alcohol and marihuana: comparative dose effect profiles in humans*. Pharmacology Biochemistry and Behaviour 31: 649-655

Huestis M A, Sampson A H, Holicky B J, Henningfield J E and Cone E J (1992). *Characterisation of the absorbtion phase of marijuana smoking*. Clinical Pharmacology and Therapeutics 52: 31-41

Huestis M A (1999). *Pharmacokinetics of THC in inhaled and oral preparations, in marihuana & medicine*. Humana Press, Totowa, N J, 105-116

Ingram D, Sawyer B and Hope S (2000). *Recreational drugs and driving, system three national survey conducted for Scottish Executive Central Research Unit.*

Jaffe J H (1990). *Drug addiction and drug abuse*. In: Goodman and Gilman's The Pharmacological Basis of Therapeutics, pp. 284-324, Pergamon Press, New York.

Jones R T (1986). *Pharmacology of cannabinoids*. US Department of Justice, Proceedings of the international symposium on driving under the influence of alcohol and/or drugs.

Keliher E (1997). *Grandpa's marijuana handbook – a user guide for ages 50 and up*. Pedagogue Press, San Diego, CA.

Kruger H P and Berghaus G (1995). *Behavioural effects of alcohol and cannabis: can equipotencies be established?* Proceedings of 13th International Conference on Alcohol, Drugs and Traffic Safety – T95. Adelaide, NHMRC Road Accident Research Unit. University of Adelaide, pp. 410-415.

Lindgren J, Ohlsson A, Agurell S, Hollister L and Gillespie H (1981). *Clinical effects and plasma levels of D9-tetrahydrocannabinol (D9-THC) in heavy and light users of cannabis*. Psychopharmacology 74: 208-212

Manno J E, Kiplinger M D, Scholz N and Forney R B (1971). *The influence of alcohol and marijuana on motor and mental performance*. Clinical Pharmacology and Therapeutics 12: 202-211.

Marks D F and MacAvoy M G (1989). *Divided attention performance in cannabis users and non-users following alcohol and cannabis separately and in combination*. Psychopharmacology 99: 397-401

Niessink R (2000). Netherlands Institute of Mental Health and Addiction, Utrecht

Ohlsson A, Lindgren J E, Wahlen A, Agurell S, Hollister L E and Gillespie H K (1980). *Plasma delta-9-tetrahydrocannabinol concentrations and clinical effects after oral and intravenous administration and smoking*. Clinical Pharmacology and Therapeutics 28(3), 409-415

Peck M A (1995). *Book review: influence of marijuana on driving by HWJ Robbe*. Journal of Psychoactive Drugs, 27: 187-191.

Perez-Reyes M, Hicks R E, Bumberry J, Jeffcoat A R and Cook C E (1988). *Interaction between marijuana and ethanol: effects on psychomotor performance*. Alcoholism: Clinical and Experimental Research, 12: 268-276.

Perez-Reyes M, Di Guiseppi S, Davis K H. Schindler V H and Cook C E (1982). Comparison of effects of marihuana cigarettes of three different potencies. Clinical Pharmacology and Therapeutics 31(5) 617-624.

Perez-Reyes M, White W R, McDonald S A, Hicks R E, Jeffcoat A R and Cook C E (1991). *The pharmacologic effects of daily marijuana smoking in humans*. Pharmacology, Biochemistry and Behaviour 40: 691-694.

Perez-Reyes M (1999). *The psychological and physiological effects of active cannabinoids, in marihuana & medicine*. Humana Press, Totowa, N J, 245-252.

Richardson N J, Rogers P J, Elliman N A and Odell R J (1995). *Activation-deactivation checklist*. Pharmacology, Biochemistry and Behaviour 52: 313-320.

Riedel W (1998). *Mechanisms of drug induced impairment.* A dimensional approach, Human Psychopharmacology, Clinical & Experimental, 13, No. S2, S58

Robbe H (1994). *Influence of marijuana on driving*. University of Limburg, Maastricht, The Netherlands: Institute for Human Psychopharmacology.

Robbe H (1998). *Marijuana's impairing effects on driving are moderate when taken alone but severe when combined with alcohol*. Human psychopharmacology clin. Exp. 13: S70-S78.

Robbe H and O'Hanlon J (1999). *Marijuana, alcohol and actual driving performance*. NHTSA Report DOT HS 808 939

Sexton B F (1997). *Validation trial for testing impairment of driving due to alcohol*. TRL Report TRL226. TRL Limited, Crowthorne.

Starmer G A and Bird K D (1984). *Investigating drug-ethanol interaction*. British Journal of Pharmacology, 18: 27S-35S.

Sticht G and Kaferstein H (1995). *Pharmacokinetic evaluation of published studies on controlled smoking of marijuana*. Proceedings of 13th International Conference on Alcohol, Drugs and Traffic Safety – T95. Adelaide, NHMRC Road Accident Research Unit. University of Adelaide, pp. 397-402.

Sutton L R (1983). *The effects of alcohol, marijuana and their combination on driving ability*. Journal on Studies of Alcohol, 44: 438-445.

Tashkin D P, Gliederer F, Rose J, Potter C, Hui K K, Yu J L and Wu T (1991a). *Effects of varying marijuana smoking profile on deposition of tar and absorption of Co and Δ^9-THC*. Pharmacol. Bio and Behav 40: 651-656.

Tashkin D P, Gliederer F, Rose J, Chang P, Hui K K, Yu J L and Wu T (1991b). *Tar, Co and Δ^9-THC delivery from the 1st and 2nd halves of a marijuana cigarette*. Pharmacol, Bio and Behav 40: 651-656.

Tunbridge R J (1998). *Drugging and driving*. In G B Grayson (Ed) Behavioural Research in Road Safety VIII. TRL Limited, Crowthorne.

Tunbridge R J, Keigan M and James F J (2000). *Recognising drug use and drug related impairment in drivers at the roadside*. TRL Report TRL464, TRL Limited, Crowthorne.

Turner, C E, Elsohly M A and Boeren E G (1980). *Constituents of cannabis sativa*. A review of the natural constituents. Journal of Natural Products, 43: 169-234.

Ward N J and Dye L (1999). *Cannabis and driving: a review and a commentary*. Road Safety Research Report No 12, DETR, London.

Wu T C, Tashkin D P, Djahed B and Rose J E (1988). *Pulmonary hazards of smoking marijuana as compared with tobacco*. N. Eng J Med 318: 347-351.

Zancy J P, Chait L D (1988). *Breathhold duration and response to marijuana smoke*. Pharmacology, Biochemistry and Behaviour 33: 481-484.

Zimmerman E G, Yeager E P, Soar J R, Hollister L E and Reeve V C (1983). *Measurement of D9-tetrahydro-cannabinol (THC) in whole blood samples from impaired motorists*. Journal of Forensic Sciences, 28: 957-962.

Appendix A: Comparison of sample with other cannabis users

In order to investigate how typical the cannabis trial study volunteers were of general regular cannabis users, the group were compared with a sample of regular users from the West Midlands. A questionnaire regarding use of cannabis and other drugs had been developed by Kay Wright who used this to obtain a profile of the typical cannabis user and had been administered to a sample of 90 or so users. Participants who attended for screening were asked to complete this questionnaire, which was contained within the screening document – Appendix D. Data on drug-use history, and attitudes and behaviour towards drink/drug-driving were collected from both groups using the same questionnaire. The questionnaire provided a further method of checking the suitability of potential participants.

Questionnaire development and distribution

A pilot questionnaire was devised following a detailed interview with a daily cannabis/alcohol user who reported driving whilst under the influence of both drugs. The questionnaire was then screened using three daily cannabis-using volunteers: (1) the original interviewee; (2) a PhD final-year student and (3) a marketing manager.

After feedback and revision, 80 questionnaires were distributed to a population of regular cannabis users of which 49 were returned, and 100 questionnaires were distributed amongst a group of second-year undergraduate students in the West Midlands, of which 41 were returned.

A relatively small percentage of students smoked cannabis on a regular basis, and so responses made by the trial participants were only compared with the response data from the regular cannabis users. Furthermore, as trial participants were all male, female regular cannabis users were excluded in the analysis. The regular cannabis user comparison group therefore comprised of 29 males. Main areas of comparison were: (1) drug history (e.g. extent of cannabis and alcohol use); (2) the number of respondents who actually drive under the influence of both drugs (alone and in combination), (3) attitudes towards driving under the influence of alcohol and cannabis (e.g. beliefs about the impairing effect of both drugs on driving ability); and (4) the number of respondents who have been stopped/charged for, and deterred from drink/drug-driving.

Characteristics of questionnaire respondents

Table A1 clearly shows similarities between group characteristics. The trial participants were a similar age to the regular cannabis users. Furthermore, they started smoking cannabis at a similar age, and consumed similar amounts of alcohol on a weekly basis. Other drug use is relatively lower amongst the trial participant sample group, with the exception of ecstasy (see Table A2).

History of cannabis and alcohol use

Similarities in cannabis use were found between groups. All trial participants smoked cannabis on at least a weekly basis compared with 75.8% of the regular cannabis users.

Table A1 Characteristics of volunteers

	Regular cannabis users n=29	*Trial participants n=15*
Age	29.6 ± 6.64	27.0 ± 7.52
Alcohol drinkers	96.6%	100%
Units of alcohol per week	24.4 ± 13.61	18.7 ± 7.89
Age started using cannabis	16.6 ± 2.66	16.7 ± 1.72
Drivers	29 (100%)	15 (100%)
Months driving	115.9 ± 83.85	106.8 ± 85.37
Use other drugs	82.7%	46.7%

Table A2 Percentage of volunteers who have used other illicit drugs

Drugs	*Regular cannabis users (n=29)*	*Trial participants (n=7)*
Ecstasy	58%	72%
Amphetamine	62%	20%
Cocaine	19%	13%
Hallucinogens	21%	7%

The majority of both groups had smoked at this frequency for 12 months or over (regular cannabis users 82.8%, trial participants 100%). A similar pattern was found in the number of cannabis cigarettes smoked, with the majority smoking three or more per occasion (regular cannabis users 51.7%, trial participants 73.3%).

Patterns of alcohol use, alone and combined with cannabis, were also similar between groups. 100% of the regular cannabis users who drank alcohol, and 87% of the trial participants, drank on at least a weekly basis. The remaining data show that 13% of the trial participants drank alcohol monthly. All trial participants combined alcohol with cannabis, compared with 93.1% of the regular cannabis users. Trial participants combined the two drugs on at least a weekly basis in 73% of cases compared with 60.8% regular cannabis users.

Drink/drug–driving behaviour

Table A3 shows that a higher percentage of trial participants drive after consuming cannabis compared with regular cannabis users, and slightly fewer trial participants drive after consuming a quantity of alcohol above legal limit for safe driving (4+ units). However, overall differences were small, and a similar pattern of driving behaviour is apparent (see Figures A1 and A2). Furthermore, fewer trial participants (46.7%) drive after combined use of cannabis and alcohol (20% weekly, 6.7% monthly) compared with 62.1% of the regular cannabis users (13.8% weekly, 10.3% monthly).

Drink/drug-driving attitudes

The majority of respondents from each sample consider their driving to be either very much impaired (31.0%

Table A3 Percentage of volunteers who report driving under the influence of alcohol and cannabis

Group	*Alcohol (Above 4 Units)*	*Alcohol (Below 4 Units)*	*Cannabis*
Regular cannabis users	24.5%	63.3%	81.3%
Trial participants	20.0%	80.0%	93.3%

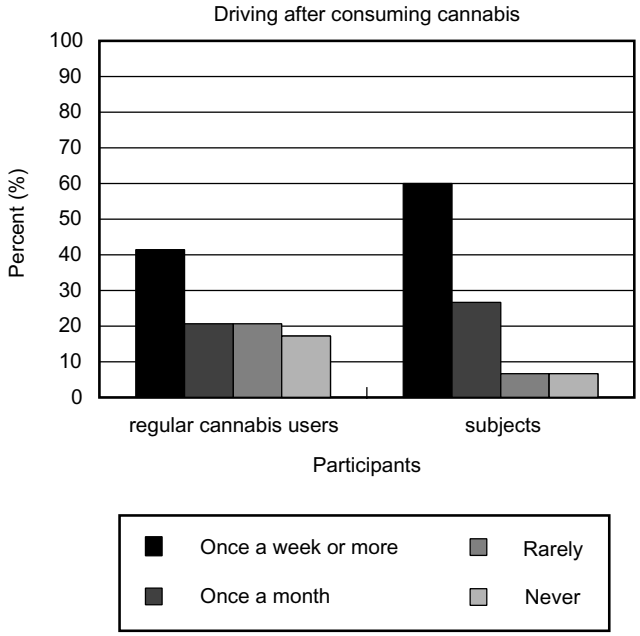


Figure A1 Percentage of regular cannabis users (RCU), and trial participants that drive after consuming cannabis

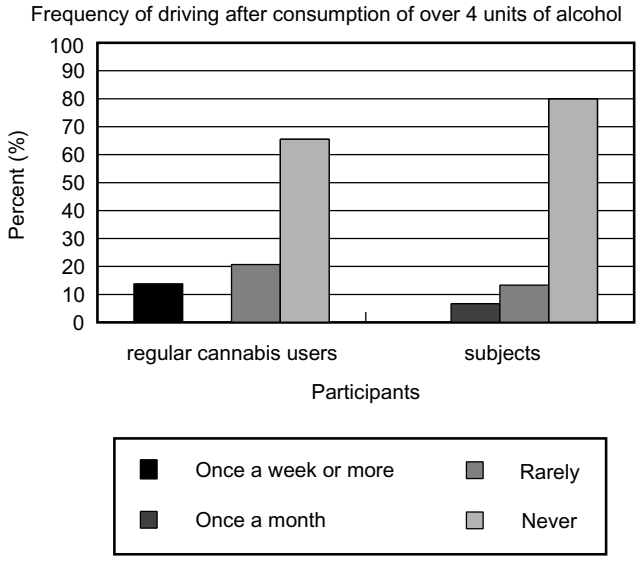


Figure A2 Percentage of regular cannabis users (n=29) and trial participants (n=15) who drive after consuming over 4 units of alcohol

regular cannabis users, 53.3% trial participants) or slightly impaired (62.1% regular cannabis users, 40% trial participants) by 4+ units of alcohol. However, one trial participant believed driving was not at all impaired, and one regular cannabis user believed driving was improved. Similarities between groups in attitudes towards driving after consuming cannabis, and related driving behavior were also found. 79.2% of the regular cannabis users and 86.7% of the trial participants believed cannabis impaired driving. However, the majority thought their driving was only slightly impaired (65.5% regular cannabis users, 80% trial participants).

Despite these attitudes towards drink and drug driving, incidences of this behaviour (particularly after the consumption of cannabis) is high, and the pattern is similar between groups (see Table A4). Drug driving in Table A4 refers to the situation when the driver had been taking drugs and was stopped by the Police, however they were not charged. This contrasts to the similar situation when they had been drinking alcohol and were stopped and were often charged. This is presumably because detecting alcohol, from the smell or via a breath test, is far easier than detecting drug use.

Table A4 Number of volunteers (and %) stopped/charged for and deterred from drink/drug driving

	Regular cannabis users (n=29)		*Trial participants (n=15)*	
	Drink -driving	*Drug -driving*	*Drink -driving*	*Drug -driving*
Stopped	11 (38%)	12 (41%)	5 (33%)	10 (67%)
Charged	4 (14%)	0 (0%)	3 (20%)	0 (0%)
Deterred	5 (17%)	2 (7%)	4 (27%)	1 (7%)
Others	9 (31%)	15 (52%)	3 (20%)	4 (27%)

Drink/drug-driving incidences

The number of respondents stopped and/or charged for, and deterred from, drink/drug-driving was remarkably similar between groups. Table A4 clearly shows that, although a greater number of respondents have been stopped for drug-driving, or a least stopped whilst under the influence of cannabis, none were charged, and only 2 regular cannabis users and 1 trial participant were deterred from repeating the behaviour. In comparison, 4 of 6 regular cannabis users and 3 of 5 trial participants were charged for drink driving. Furthermore, being stopped for drink-driving deterred 5 of the regular cannabis users and 4 of the trial participants.

In conclusion, the results show that the trial participant groups used for this trial study were fairly typical of a more general population of regular cannabis users in their characteristics and history of alcohol and cannabis use, as well as in their attitudes and behaviour towards drink/drug-driving.

Appendix B: Report on the sobriety tests

Introduction

A police officer may arrest a person if he has reasonable grounds to suspect that the person has been driving or attempting to drive whilst unfit through drugs (Section 4 (1) of the Road Traffic Act 1988 as amended by the Road Traffic Act 1991 (RTA)). Being unfit is defined in section 4(5) of the Road Traffic Act 1988 '*…a person shall be taken to be unfit to drive if his ability to drive properly is for the time being impaired*.' At the police station following such an arrest a forensic medical examiner (FME) will be called to examine the person.

The aim of this examination is twofold. Firstly to ensure that the person is fit to be in a police station - that there is no evidence of injury (e.g. head injury following a road traffic accident) or a medical condition (e.g. hypoglycaemia) requiring urgent treatment - and secondly to determine whether the driver is impaired to drive or whether there is a condition that might be due to a drug.

In order for the police to require a specimen (blood or urine) for analysis (Section 7 (3) (c) RTA) the FME needs to advise the police officer that the condition of the person required to provide the specimen might be due to a drug (Cole v DPP).

In forensic circles there has been controversy as to whether the FME had to certify impairment before the police could lawfully request a blood sample for analysis (Stark & Rogers 1995, Ley 1996, Corre 1996). Case law has now clarified this issue so that police can lawfully request a blood sample for analysis even if the person is not demonstrably impaired at the time of the FME's examination (L v DPP 1998, Rogers & Stark 1999).

Furthermore the CPS has recently issued guidance (Stark et al., 2000) on the relevant question 'might a suspect's condition be due to some drug?' The FME's advice to the police officer can be based upon conclusions drawn not only from his or her own examination of the suspect but also from relevant information gleaned from the suspect or the police concerning earlier events. However exactly what constitutes a 'condition due to a drug' remains an issue for debate amongst forensic physicians.

At present there is no nationally agreed examination protocol for FMEs to use when carrying out such assessments, although in Scotland a F97 Medical Examination Form is used and other forms have been recommended (Fleming & Stewart 1998, Wall & Karch 2000).

In this project two registered medical practitioners (experienced Forensic Medical Examiners) examined the participants and carried out a comprehensive physical examination to see whether the suggested standard 'impairment' tests currently used were effective in detecting impairment due to cannabis.

Comprehensive physical examination

A standardised examination form was used adapted from the Police Research Group report (Fleming & Stewart 1998) (see Figure B1). This included tests covering pupil size, and reaction to light; eye movements; walk and turn test; one leg stand; finger-nose test; Romberg's test with internal clock and an example of writing. The physical examination included a comment on the general demeanour and behaviour of the individual and examination of speech, pulse, temperature, ears, eyes, heart, lungs, blood pressure and reflexes. The physical signs of cannabis use are summarised in Table B1.

Table B1 Signs of cannabis use related to physical examination

Effects	*Physical signs*	*Examination parameters*
Psychological	Euphoria, anxiety, disinhibition with spontaneous laughter, verbosity.	Comment on general demeanour and behaviour.
Perception	Hallucinations, distortion of time sense.	Internal clock.
Sedative	Sedation, relaxation.	Conscious level.
Cognition	Impairment of short-term memory and concentration, confusion, disorientation, attention span reduced and user's ability to process information impaired.	Walk and turn test. One leg stand. Finger nose test.
Motor function	Inco-ordination, ataxia, dysarthia, tremulousness,weakness, ability to perform complex motor tasks, balance and stability impaired.	Speech. Walk and Turn test. Finger nose test. One leg stand. Romberg's test.
Cardiovascular	Tachycardia. Increased blood pressure.	Pulse. Blood pressure.
Eye	Conjunctival injection. Anisocoria. Change in pupil size. Sluggish reaction to light. Horizontal nystagmus. Vertical nystagmus. Absent of convergence.	Pupillometer. Pupil reaction to direct light stimulus. Eye movements.
Other	Flushing. Change in body temperature.	Skin appearance. Temperature.

The doctors were asked to conclude whether in their opinion at the time of the examination the individual was 'impaired' or whether there was 'a condition' that might be due to the presence of a drug. No formal definitions have been agreed for what constitutes 'a condition' or 'impairment'.

General examination

General demeanour and behaviour:	Normal	Euphoric	Anxiety	Verbosity
	Sedation	Hallucination		
State of clothing:	Normal			
Speech: (ask "Have you been well over the last week?")	Normal	Slurred		
Condition of mouth:	Normal			
Pulse: rate and character		b.p.m.	Normal	Bounding
Temperature:		^{o}C		
State of tongue:	Normal			
Breath:	Normal			
Ears:	Normal	Wax	TM Red	
Heart:	Normal			
Blood pressure:				
Lungs (added sounds):	Normal	Wheeze		
Reflexes:	Normal	Increased	Decreased	
Eyelids red or swollen?	Normal			
Conjunctivae?	Normal	Injected		
Evidence of squint etc?	Normal			
Any gross visual defect?	Normal			
Glasses?	Yes	No		

Figure B1 Cannabis study medical examination form

Impairment testing

Pupil size (using card pupillometer)		mm
Anisocoria	Absent	Present
Pupillary reaction to direct light stimulus	Normal	Sluggish
Horizontal gaze nystagmus	Absent	Present
Vertical gaze nystagmus	Absent	Present
Convergence	Present	Absent

Walk and turn test (9 steps)	Start too soon	Yes	No
	Stops walking	Yes	No
	Misses heel/toe	Yes	No
	Raises arms	Yes	No
	Starting balance	Impaired	Normal
	Turns improperly	Yes	No
	Steps off line	Yes	No
	Correct step count	Yes	No
	Fails instructions	Yes	No

		Right		Left	
One leg stand	Sways	Y	N	Y	N
	Raises arms	Y	N	Y	N
	Hops	Y	N	Y	N
	Puts foot down	Y	N	Y	N
	Fails instructions	Y	N	Y	N

Finger nose test (eyes closed)	Touch tip of nose	Yes	No
Left / Right / Left / Right / Right / Left	Correct hand	Yes	No
	Sways	Yes	No
	Fail instructions	Yes	No

Romberg test – body sway	Yes	No

Internal clock – 30 seconds estimates at		Time
(allow 10 seconds either way)	Normal	Abnormal

Writing: copy this

1.Remarks (include any unsolicited remarks regarding volunteer's feelings)

2.Conclusion

Impaired?	Yes	No
Condition might be due to a drug?	Yes	No

Figure B1 (Continued) Cannabis study medical examination form

Guide to the interpretation of results

Physical examination

Although the participants had been screened and were healthy male volunteers. It was important to exclude any recent or current medical problem that may have affected the interpretation of any tests used to assess fitness to drive e.g. a current ear infection which may have an effect on balance (Romberg's test). The physical examination is also important to document physical signs (physiological effects) of a drug e.g. tachycardia, conjunctival reddening. It was decided that we would not ask them specifically how they felt at the time of the exam but that any unsolicited comments would be noted. Abnormalities included a pulse rate of 90 beats per minute or over and a blood pressure with a diastolic of 90 or over, and total systolic of 100 plus their age. Readings below these limits would be considered normal.

The 'impairment' tests

In general for each of the tests below the participant was reminded once of the instructions if they initially failed to perform the test correctly. Participants were allowed to fail one parameter of one of the 'impairment tests' but if they failed two or more parameters or one parameter in a number of tests this was considered abnormal. At this stage of impairment testing, where standards are still being developed, it was not thought appropriate to be more specific than this. The 'impairment' tests are reported with failures over the total number of parameters measured, e.g. in the finger nose test if the participant failed all four parameters this would be reported as 4/4.

Pupillary examination

Pupil size and equality was assessed by comparing the size of the pupils against the pupillometer on a card held up at the side of the face. The normal range for pupil size was 3.0-5.0mm given the lighting conditions (bright) of the room when compared to roadside testing. At the same time an evaluation of the pupillary reaction to a direct light stimulus was performed.

Eye movements

The presence of lateral nystagmus, vertical nystagmus and convergence were sought. A stimulus is held about 12-15 inches away from the face and the participant is instructed to follow the stimulus with their eyes keeping their head still. The stimulus is moved from the centre of the nose to the right and then the left (to check for horizontal nystagmus) and up and down (to check for vertical nystagmus). The stimulus should be moved to the right or left until the white of the eye is no longer observed but not out of the person's line of site. To examine for convergence (having excluded a squint – weak eye muscles) the participant is again asked to follow the stimulus with their eyes, keeping their head still, the stimulus is brought in towards the nose. If one of the eyes drifts away or fails to converge non-convergence is present.

Walk and turn test

The participant is instructed to place his left foot on the line and then to place the right foot on the line in front of the left foot, with the heel of the right foot in contact with the toe of the left foot. The participant is then told to put his arms at his sides and take nine heel to toe steps along the line, turning around and take a further nine heel to toe steps back along the line.

Signs of impairment include whether the individual (9 parameters):

- starting balance is impaired;
- starts too soon;
- stops walking;
- misses heel/toe;
- raises arms;
- turns improperly;
- steps off line;
- counts steps incorrectly;
- fails to follow instructions.

One leg stand

The participant stands with his feet together and arms by his sides and is then asked to raise his right foot 6 - 8 inches off the ground keeping his leg straight. The toes must be pointing forward and the foot parallel to ground. The participant should keep his arms by his sides and look at the raised foot while counting 15 seconds, as 1001, 1002, 1003 etc. to 1015. The test is then repeated for the left foot.

Signs of impairment include whether the individual (5 parameters for each side):

- sways;
- raises arms;
- hops;
- puts foot down;
- fails to follow instructions.

Finger to nose test (eyes closed)

The participant is instructed to stand with his feet together and arms at his sides and tilt his head back slightly. The participant should then extend both hands, palm side up, out in front and make a fist. The index finger of both hands is then extended and keeping the fingers in that position, he places his hands at his sides, with the palm side forward. The examiner then says either left or right to indicate which hand should be raised directly in front and the tip of the nose touched with that index finger. The hand is then lowered until the next is indicated. The hands are called out in the following order: left, right, left, right, right, left.

Signs of impairment include whether the individual (4 parameters):

- touches tip of nose / misses tip of nose;
- uses correct hand / uses incorrect hand;
- sways;
- fails to follow instructions.

Romberg test

This test is used to evaluate the participant's internal clock and body sway. The participant is instructed to stand up straight with his feet together and arms by his sides. The participant must tilt his head back slightly, and close his eyes while estimating to himself that 30 seconds have elapsed and then bring his head forward and say 'stop'. The test is abnormal if the body sways (Romberg's positive) and the timing is less than 20 seconds or more than 40 seconds.

Handwriting

Writing is a useful analysis tool in the assessment of alcohol impairment and so it was decided to add a specimen of handwriting to the overall evaluation. The participants were asked to copy:

> 'A football team has bounced back to victory thanks to jelly babies.
>
> Players chew on the sweets every Saturday before a game.'
>
> (Smith E. Jelly Well Played. The Sun, Monday December 13 1999 pp.3)

Writing was considered abnormal if the participant started in the wrong place and if there were mistakes in the flow of the writing. An example of handwriting is attached from the same participant from each of his 4 visits. In this limited trial of handwriting no substantial effect on handwriting was observed.

Results

56 examinations were performed and on 11 occasions participants were found to be impaired, a further 21 were found to have a condition that could be due to a drug, but were not impaired, 24 were normal with 3 participants having 'normal' examinations throughout the three doses of cannabis. It should be noted that the presence of a condition and impairment are not mutually exclusive. Tables B2, B3 & B4 give the classifications with the dose and abnormal examination findings and any unsolicited comments. The tables also show the maximum Δ^9-THC content available in each cigarette, which was estimated by weighing the portion that was not smoked.

Discussion

One of the main limitations in performing the examinations was time pressure due to the protocol of the main study. In the custodial situation the doctor has as much time as is required to assess an individual's fitness to drive and exclude disease and injury. This will involve taking a history from the arresting officer, information from the custody officer as well as the detailed history from the individual and general physical examination. Complex cases may take over half an hour.

When the results were reviewed it was clear that because of the lack of formal definitions for a 'condition' and 'impairment' the two medical practitioners had not used the same criteria to conclude whether a particular individual had a 'condition' or was 'impaired'.

Table B2 Participants considered to be impaired

Ref No Dr	*Dose mg THC*	*General exam*	*Impairment testing*
001 Jak 1 KE	High 22.64	Pulse 166 bounding BP 151/93 Increased reflexes Conjunctivae injected	Pupils 6.5mm sluggish reaction Horizontal nystagmus Walk and turn 6/9 One leg stand L 3/5 R 2/5 Finger nose 2/4 Romberg's positive Internal clock 20 seconds Tremor Writing abnormal
001 Jak 3 KE	Low 11.53	Pulse 121 BP 142/101 Conjunctivae injected	Pupils 4.0mm sluggish reaction Walk and turn 2/9 One leg stand L 3/5 R 4/5
009 Gar 3 MS	High 18.50	Giggling Pulse 109 bounding BP 148/90 Conjunctivae injected	Pupils 4.5mm sluggish reaction Walk and turn 3/9 One leg stand R 2/5 L 1/5 Finger nose 1/5
010 Jim 2 MS	High 17.38	BP 169/95 Conjunctivae injected	Pupils 5.0mm sluggish reaction Walk and turn 1/9 One leg stand R 1/5 L2/5
010 Jim 1 MS	Low 9.81	Pulse 115 bounding Blood pressure 133/95	Pupils 4.5mm sluggish reaction Anisocoria Walk and turn 1/9 One leg stand R 3/5 L 3/5 Finger nose 1/4
014 Ric 4 MS	Resin 4.18	Giggling Pulse 132 bounding BP 116/82 Conjunctivae injected	Pupils 4.5mm sluggish reaction One leg stand R 2/5 L 2/5 Finger nose 1/4
030 Ros 1 MS	High 16.82	Pale Withdrawn Increased reflexes Conjunctivae injected	Pupils 3.5mm sluggish reaction Horizontal nystagmus One leg stand R 2/5 L 1/5 Romberg's positive *'I feel stoned. I'm glad I'm not like this when stopped by the police'*
031 Tim 2 MS	High 18.05	Pulse 162 BP 152/97 Conjunctivae injected	Pupils 5.5mm sluggish reaction Walk and turn 1/9 Romberg's positive Internal clock 20 seconds
032 Mar 3 MS	High 20.16	Quiet Subdued Pulse 121 bounding BP 146/83 Conjunctivae injected	Pupils 5.5mm sluggish reaction Walk and turn 1/9 One leg stand R 2/5 L 1/5 Finger nose 1/5 Romberg's positive
032 Mar 2 MS	Low 11.80	Pulse 100 BP 138/95 Conjunctivae injected	Pupils 5.5 sluggish reaction Walk and turn 2/9 One leg stand R 2/5 L2/5 Romberg's positive
033 And 2 KE	High 18.96	Pulse 112 BP 146/101 Conjunctivae injected	Pupils 5.5mm Horizontal nystagmus Walk and turn 1/9 One leg stand R 3/5 L 3/5 Romberg's positive

Table B3 Participants considered to have a 'condition'

Ref No Dr	*Dose mg THC*	*General exam*	*Impairment testing*
001 Jak 4 MS	Resin 5.33	Pulse 136 bounding BP 129/90 Conjunctivae injected	Pupils 5.5mm sluggish reaction Walk and turn 1/9 Flushed
005 Mar 1 KE	High 14.95	Throat inflamed Pulse 119 bounding BP 125/77 Conjunctivae injected	Finger nose 2/4 Poor concentration with writing
006 Jas 3 MS	High 20.32	BP 148/88 Conjunctivae injected	Pupils 5.5mm sluggish reaction One leg stand R 2/5 L 2/5 Finger nose 1/5
006 Jas 4 MS	Resin 5.83	BP 146/86 Conjunctivae injected	Pupils 4.0mm sluggish reaction One leg stand R 1/5 L2/5
010 Jim 4 MS	Resin 2.96	BP 145/93	Pupils 4.0mm sluggish reaction One leg stand R 1/5 Finger nose 1/4
009 Gar 2 MS	Low 11.36	Euphoric Giggling Pulse 121 bounding BP 165/100 Conjunctivae injected	Pupils 4mm sluggish reaction Internal clock 40 seconds
009 Gar 4 MS	Resin 2.70	BP 155/101 Conjunctivae injected	Pupils 4.5mm sluggish reaction Walk and turn 1/9 One leg stand 1/5 Finger nose 1/4
014 Ric 1 MS	Low 9.79	Giggling Pulse 92 BP 139/86 Conjunctivae injected	Pupils 3.5mm sluggish reaction Convergence absent Walk and turn 1/9 One leg stand R 1/5 Romberg's positive Internal clock 18 seconds
014 Ric 2 MS	High 17.01	Pulse 123 BP 123/85 Conjunctivae injected	Pupils 4.5mm sluggish reaction Finger nose 1/5 Internal clock 45 seconds
014 Ric 3 MS	Plac. 0.03	Pulse 107 BP 126/89 Conjunctivae injected	Finger nose 1/5
015 Ian 1 MS	High 18.96	Pulse 107 BP 112/94 Conjunctivae injected	Pupils 6.0mm sluggish reaction
015 Ian 3 MS	Low 11.63	Pulse 110 BP 141/110 Conjunctivae injected	Pupils 6.5mm sluggish reaction
015 Ian 4 MS	Resin 4.75	Pulse 112 bounding BP 151/85	Pupils 5.0mm sluggish reaction Romberg's positive
023 Dav 1 MS	High 18.24	Pulse 113 bounding BP 162/91 Conjunctivae injected Writing abnormal	Internal clock 50 seconds
023 Dav 3 MS	Low 10.46	Pulse 105 BP 155/81 Conjunctivae injected	Pupils 5.0mm sluggish reaction Anisocoria Finger nose 1/5 Romberg's positive
023 Dav 4 MS	Resin 5.75	Pulse 92 bounding BP 126/96 Conjunctivae injected	Pupils 5.0mm sluggish reaction Walk and turn 1/9 Finger nose 1/5 Romberg's positive
031 Tim 1 MS	Low 10.64	Pulse 135 bounding BP 159/124 Increased reflexes Conjunctivae injected	Pupils 5mm sluggish reaction Absence of convergence Walk and turn 1/9 One leg stand R 1/5 L 1/5
031 Tim 3 MS	Plac. 0.03	BP 141/111	Pupils 5.5mm sluggish reaction
031 Tim 4 MS	Resin 1.76	Pulse 90 BP 172/95 Conjunctivae injected	Pupils 4.0mm sluggish reaction
032 Mar 4 MS	Resin 0.30	Pulse 101 BP 143/74	Pupils 4.5mm sluggish reaction One leg stand L 2/5 R 5/5 Finger nose 1/5
033 And 3 MS	Low 13.45	Giggling Pulse 100 bounding BP 156/99 Conjunctivae injected	Pupils 6.0mm sluggish reaction Walk and turn 2/9 One leg stand R 1/5 Romberg's positive Flushed

Table B4 Participants considered normal (not impaired with no condition)

Ref No Dr	*Dose mg THC*	*General exam*	*Impairment testing*
001 Jak 2 KE	Plac. 0.03	Increased reflexes	
003 Nik 1 MS	Plac. 0.03	BP 161/95	
003 Nik 2 MS	Low 11.61	BP 185/92	Pupils 5.0mm sluggish reaction
003 Nik 3 MS	High 16.98	BP 180/100	Walk and turn 1/9
003 Nik 4 KE	Resin 14.78	BP155/104 Conjunctivae injected	
006 Jas 1 MS	Plac. 0.03	Pulse 90 bounding BP 137/96	
006 Jas 2 MS	Low 10.68		One leg stand L 1/5 Romberg's positive
010 Jim 3 MS	Plac. 0.03	BP 141/74	Walk and turn 2/9 Romberg's positive *'I've had placebo'*
009 Gar 1 MS	Plac. 0.03	BP 150/99	Walk and turn 1/9 One leg stand L 2/5 R 2/5
011 Gar 1 MS	Low 9.95	Pulse 108 BP 147/105	Anisocoria Internal clock 15 seconds
011 Gar 2 MS	High 18.69	Pulse 100 BP 145/116	Anisocoria Convergence absent
011 Gar 3 MS	Plac. 0.03	BP 167/117	
011 Gar 4 MS	Resin 2.40	BP 156/59	Anisocoria Internal clock 40 seconds
015 Ian 2 MS	Plac. 0.03	Pulse 105	Finger nose 1/5
023 Dav 2 MS	Plac. 0.03	Conjunctivae injected	
030 Ros 2 MS	Plac. 0.03		
030 Ros 3 MS	Low 10.64	Pulse 94	
030 Ros 4 MS	Resin 6.65	Conjunctivae injected	
032 Mar 1 MS	Plac. 0.03		
033 And 1 KE	Plac. 0.03	BP 140/96	*'I don't think I had the real stuff'*
004 Jam 1 KE	Low 11.66	BP 159/104 Increased reflexes Conjunctivae injected	Pupils 4mm sluggish reaction One leg stand L 1/5 Finger nose 1/4
004 Jam 2 KE	High 16.77	Increased reflexes Conjunctivae injected	Pupils 4mm sluggish reaction One leg stand L 2/5 Finger nose 1/4
004 J am 3 KE	Plac. 0.03	BP 149/82	
004 Jam 4 KE	Resin 3.58	BP 135/77 Conjunctive injected	Horizontal nystagmus Walk and turn 1/9

Knight (1992) has previously noted that the degree and manifestations of 'impairment' in this context have never been satisfactorily defined and the court can take into account the evidence of the police officer, the doctor and the results of any analysis.

In any assessment of ability to drive the doctor will give the benefit of the doubt to the individual. So for example, although it is accepted that the use of cannabis results in a tachycardia, if that was the only abnormal finding with there being an alternative explanation such as anxiety, the doctor would not certify that there was 'impairment' though some may be of the opinion that this finding was consistent with 'a condition due to a drug'.

In this project the doctors made a decision on the totality of the observations that a given individual was impaired or had a condition based on the formal sobriety tests and physical examination. It was clear on review of the results that the initial classification of participants would have been different if pre-defined criteria had been used. Following discussion between the two doctors, as a basis for guidance, the following criteria for 'a condition' and 'impairment' have been deduced:

A 'condition' due to a drug may exist with at least one abnormal finding on general physical examination and two abnormalities on 'impairment tests'. However for 'impairment' to be present there *must* be abnormal findings on general physical examination *and* failure to perform three parts of at least *three* 'impairment tests'.

Using these criteria the participants would have been reclassified as follows:

17 'impaired'

20 'a condition'

19 'normal'

If a larger number of participants were formally examined using this guidance there may be scope for refining such proposed criteria.

Pupillometer

Introduction

Reported ocular effects of cannabis include abnormalities of eye movements, effects on pupil size and reaction to a light stimulus (Fraunfelder & Meyer 1989). However the effect of cannabis on pupil size is controversial. Hepler (1972) examined the pupils before smoking (2g of cannabis in a 30 minute period using an ice-cooled pipe with a THC concentration 1.5%) and at intervals of 5, 60, 150 and 300 minutes after smoking and demonstrated that the pupils tend to constrict slightly soon after smoking cannabis. Green (1982) has stated that pupillary dilation is often erroneously attributed to cannabis and suggests that this response is usually noted by law enforcement personnel and is more likely a product of fear. Certainly a report (Fleming & Stewart 1998) with guidelines for doctors on the physical findings following cannabis states that the pupil size may be normal or dilated.

In a recent study (Priemer et al., 1999), 12 healthy volunteers inhaled a joint containing 40mg THC within 10 minutes. Pupil size was measured before dosing as well as at 40 and 80 minutes. The pupil diameter tended to decrease during THC impairment. Other research (Pickworth et al., 1998) has shown that after a dose of 3.9% THC the pupil diameter decreased in size with a peak response at 30 minutes.

Method

Pupillary size was measured using a Procyon Pupillometer® Model P2000SA pre-dosing and at 30 minutes post dosing. The researchers found the Pupillometer easy to use and the participants were seated in front of the Pupillometer at such a height to look into the eyepieces at a comfortable viewing angle. Ten images of each pupil were then taken over a two second period to calculate the pupil size.

Results

The average pupil size increased from the baseline measurement at 30 minutes at both low and high dose (see Figure 21 in the main report) but was more significant with low dose.

The medical practitioners measured pupil size approximately 15 minutes post-dosing and in the 14 cases where clinical comparisons were possible over placebo the following results were obtained:

High dose	11 pupil size increased (2 decrease, 1 unchanged)
Low dose	8 pupil size increased (3 decrease, 3 unchanged)
Resin (13 cases)	3 pupil size increased (6 decrease, 4 unchanged)

Direct comparisons of the pupil size between the Pupillometer findings and the clinical findings are not possible as the conditions of measurement were different. These findings, using the Pupillometer and clinical examination, of an increase in pupil size post cannabis appear contradictory to previous research literature and requires further evaluation.

References

Cole v DPP (1988). Interpretation of Section 7 (3) (c) of the Road Traffic Act RTR 224

Corre N (1996). *Letter to the editor*. Medico-Legal Journal 64:4;198-199

Fleming P and Stewart D (1998). *Drugs and driving: training implications for police officers and police surgeons*. Police Research Group. Home Office, London.

Fraunfelder F T and Meyer S M (1989). *Drug-induced ocular side effects and drug interactions*. Agents Affecting the Central Nervous System pp130-132

Hepler R S, Frank I M and Ungerleider J T (1972). *Pupillary constriction after marijuana smoking*. American Journal of Ophthalmology 74:9:1185-1190

Knight B (1992). *The drinking driver*. In Legal Aspects of Medical Practice. Churchill Livingstone pp.31

L v DPP (1988). High Court of Justice, Queen's Bench Division 25th March 1998

Ley N (1996). *Letter to the editor*. Medico-Legal Journal 61:1;43

Pickworth W B, Fant R V and Bunker E B (1998). *Effects of abused drugs on pupillary size and the light reflex.* In Karch SB., ed. Drug Abuse Handbook. CRC Press, Boca Raton, Florida pp 266-275

Priemer F, Gappmaier A, Ruby M, Sachs H, Tutsch-Bauer E, Peschel O and Eisenmenger W (1999). *The effect of THC on the pupillary reaction*. Blutalkohol 36: 84-98

Rogers D J and Stark M M (1999). *Driving whilst unfit through drugs*. Journal of Clinical Forensic Medicine 6:166-167

Stark M M and Rogers D J (1995). *Drink driving legislation, letter to the editor*. Medico-Legal Journal 63:4;179-180

Stark M M, O'Keefe V and Rowe D (2000). *Letter to the editor*. Journal of Clinical Forensic Medicine 7:59

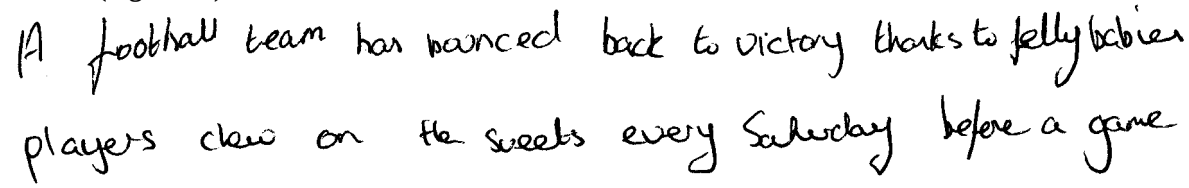
Wall I F and Karch S (2000). *Traffic medicine.* In Stark M M, ed. A Physicians' Guide to Clinical Forensic Medicine. Humana Press, Totowa, NJ pp 308-309

Glossary

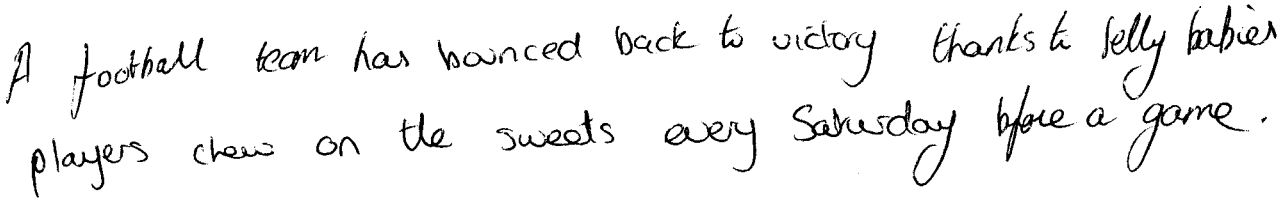
Anisocoria	unequal diameters of the pupils.
Ataxia	unsteadiness, uncoordination.
Conjunctival	reddening of the conjunctivae injection .
Convergence	the simultaneous act of both eyes coming together towards the midline.
Dysarthria	disorder of articulation, slurred speech.
Nystagmus	spontaneous rapid rhythmic eye movements in a side-to-side (horizontal) or up-and-down (vertical) direction.
Tachycardia	fast heart rate.

Example of participant's handwriting from his four visits:

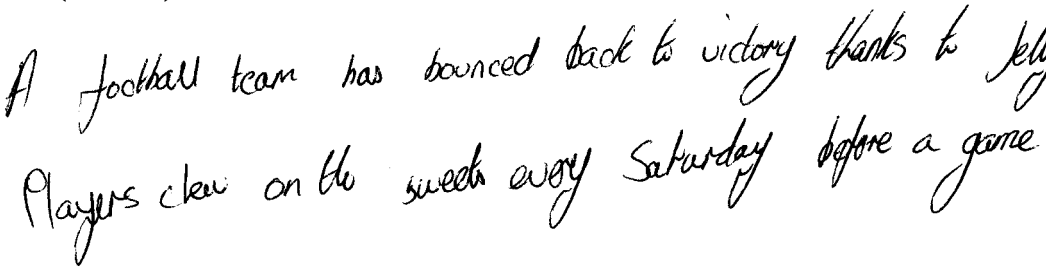
Period 1 (high dose)



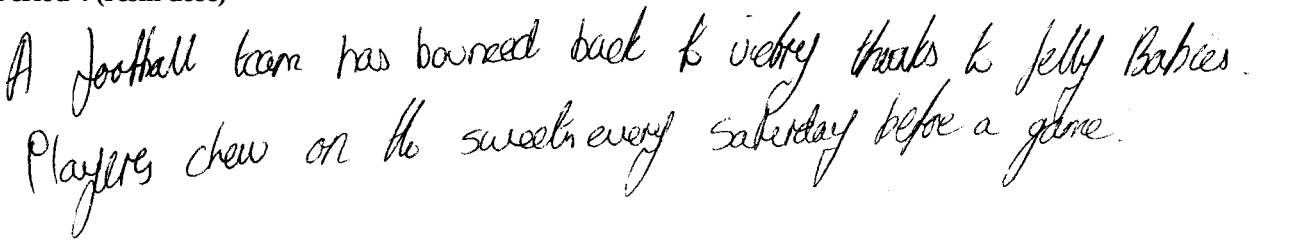
Period 2 (placebo)



Period 3 (low dose)



Period 4 (resin dose)



Appendix C: Mood questionnaire analysis

Factor analysis

A factor analysis was conducted on the mood checklist variables, using maximum likelihood as the method of extraction and a varimax rotation. Initially two factors were identified, however these factors did not make logical sense. The analysis was therefore repeated with three factors. The three factors extracted made logical sense and were given labels, as shown in Table C1.

Table C1 Factors extracted from maximum likelihood factor analysis

Feelings/signs of anxiety	*Feelings/signs of listlessness*	*Feelings/signs of wellbeing*
Increased heart rate	Dizziness	Clear
Shaking	Irritability	Alert
Bodily awareness	Sickness	Drowsy*
Palpitations	Difficulty concentrating	Calm
Anxiety	Slow	Cheerful
Loss of appetite	Tired	Difficulty remembering*
Sweating		
Tenseness		

* *Variable coded in reverse direction*

A factor analysis was also conducted using maximum likelihood as the method of extraction, however with an oblique rotation. Three similar factors were extracted. The variables 'dry mouth' and 'confidence' did not correlate with the three factors in either of the analyses, and have been analysed separately.

Reliability analyses

Reliability analyses were conducted on the three factors. For the factors identified by the varimax rotation method, the factor anxiety was significantly reliable (α= 0.90), as was the factor listlessness (α= 0.85). The factor wellbeing did not quite reach a reliability value of 0.8. However from the analysis it could be seen that removing any of the variables would not increase the reliability to above 0.8, and removing each variable individually, with the exception of one, would in fact reduce the reliability. It was observed that the squared multiple correlations for the variables in this factor were all greater than 0.3, it was therefore decided to continue analysing 'wellbeing' as a factor. An oblique rotation solution was investigated but the factors identified from the varimax rotation had slightly higher reliability significance than those of the oblique rotation, and made more logical sense.

The direction of the scale for the factors

A high score of anxiety reflects a high level of increased heart rate, shaking, bodily awareness, palpitations, anxiety, loss of appetite, sweating and tenseness. It therefore indicates that the participant was experiencing high feelings of anxiety. A high score of listlessness reflects a high level of dizziness, irritability, sickness, difficulty concentrating, slowness and tiredness. It therefore indicates that the participant was experiencing high feelings of listlessness. A high score of wellbeing reflects a high level of feeling clear, alert, calm and cheerful, and a low level of feeling drowsy and having difficulty remembering. It therefore indicates that the participant was experiencing high feelings of wellbeing and wakefulness.

Analysis of variance

A repeated measure ANOVA and the one-way ANOVA were used to analyse the data. A range of post-hoc testing was carried out by assuming that participants in the different dosing conditions were different people. The SPSS package was used for the analysis.

Analysis of the factor 'anxiety'

Repeated measures ANOVAs were conducted to identify the affects of time after dosing on the factor 'anxiety'. The data are shown in Figure C1. No significant interaction effects of time and the type of dose administered were observed. One way ANOVAs were conducted to identify the affects of the dosing types administered within each time. For the baseline measurements no significant difference were identified between the scores of 'anxiety' in each dosing type.

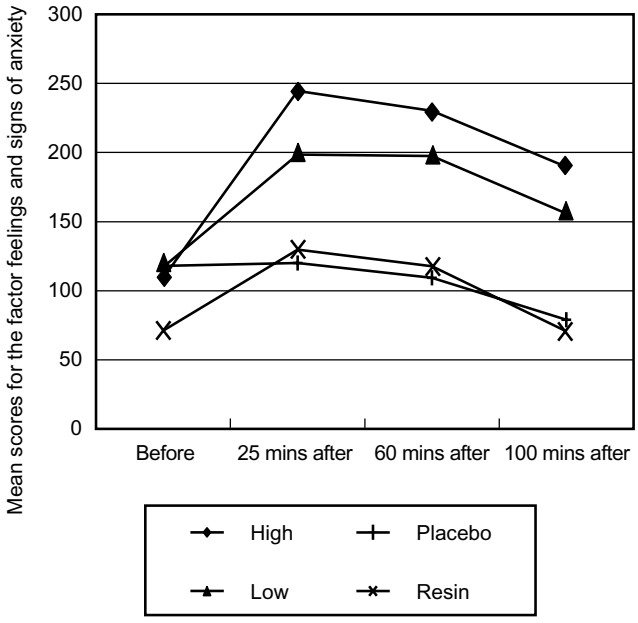


Figure C1 Summary of 'anxiety' scores

Significant differences were found at other times. The results for all dose levels are summarised in Table C2, where for example the high dose is significantly different from the placebo and resin dose 25 minutes after dosing.

Table C2 Summary of analysis for 'anxiety' factor

Comparison	*Significant differences*	*Test statistic*
Over time – compared to before dosing	More 'anxious' 25 minutes post dosing	$F_{1,52}$=48.4, p<0.001
	More 'anxious' 60 minutes post dosing	$F_{1,52}$=25.5, p<0.001
Before dosing	No differences between doses	
25-mins after dosing	Significant differences Placebo v high dose Resin v high dose	$F_{3,51}$=4.32, p<0.01 p<0.05 p<0.05
60-mins after dosing	Significant differences Placebo v high dose Resin v high dose	$F_{3,52}$=5.11, p<0.01 p<0.01 p<0.05
100-mins after dosing	Significant differences Placebo v high dose Resin v high dose	$F_{3,51}$=4.76, p<0.01 p<0.05 p<0.05

Table C3 Summary of analysis for 'listlessness' factor

Comparison	*Significant differences*	*Test statistic*
Over time – compared to before dosing	More 'listless' 25 minutes post dosing	$F_{1,52}$=15.7, p<0.001
	Interaction between dose and time at 25 minutes	$F_{3,52}$=4.53, p<0.01
	Interaction due to placebo v high dose	p<0.05
	More 'listless' 60 minutes post dosing	$F_{1,52}$=24.5, p<0.001
	Interaction between dose and time at 60 minutes	$F_{3,52}$=4.53, p<0.01
	Interaction due to placebo v high dose	p<0.05
	More 'listless' 100 minutes post dosing	$F_{1,51}$=17.3, p<0.001
	Interaction between dose and time at 100 minutes	$F_{3,52}$=4.12, p<0.05
Before dosing	No differences between doses	
25-mins after dosing	Significant differences Placebo v high dose Resin v high dose	$F_{3,52}$=5.53, p<0.01 p<0.01 p<0.05
60-mins after dosing	Significant differences Placebo v high dose Resin v high dose	$F_{3,52}$=4.11, p<0.05 p<0.05 p<0.05
100-mins after dosing	Significant differences Placebo v high dose Resin v high dose	$F_{3,51}$=3.93, p<0.05 p<0.05 p<0.05

Analysis of the factor 'listlessness'

Repeated measures ANOVAs were conducted to identify the affects of time after dosing on the factor 'listlessness'. The data are shown in Figure C1. Significant interaction effects between the time the questionnaire was administered and the type of dose administered was observed. Post-Hoc tests identified where the interactions were statistically significant.

One way ANOVAs were conducted to identify the affects of the dosing types administered. For the baseline measurements no significant difference was identified between the scores of 'listlessness' in each dosing type. Significant differences were found at other times. The results for all dose levels are summarised in Table C3.

Analysis of the factor 'wellbeing'

Repeated measures ANOVAs were conducted to identify the affects of time after dosing on the 'wellbeing' factor. The data are shown in Figure C2. Significant interaction effects between the time the questionnaire was administered and the type of dose administered was observed. Post-Hoc tests identified where the interactions were statistically significant.

One way ANOVAs were conducted to identify the affects of the dosing types administered. For the baseline measurements no significant difference was identified between the scores of listlessness in each dosing type. Significant differences were found at 25 minutes post dosing. The results for all dose levels are summarised in Table C4.

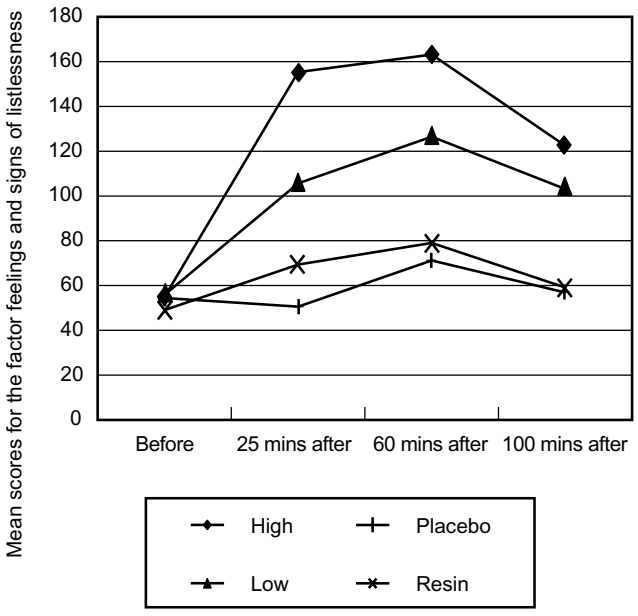


Figure C2 Summary of 'listlessness' scores

Analysis of 'confidence' and 'dry mouth' as separate variables

No significant differences were found between the levels of 'confidence' reported either between the levels of dosing or between the baseline and other times during the experiment.

Repeated measures ANOVAs were conducted to identify the affects of time after dosing on the 'dry mouth' question. Significant interaction effects between the time the questionnaire was administered and the type of dose administered was observed.

One-way ANOVAs were conducted to identify the affect on 'dry mouth' of the dosing types administered. The results for all dose levels are summarised in Table C5.

Table C4 Summary of analysis for 'wellbeing' factor

Comparison	*Significant differences*	*Test statistic*
Over time – compared to before dosing	Higher 'wellbeing' 25 minutes post dosing	$F_{1,51}$=20.3, p<0.001
	Interaction between dose and time at 25 minutes	$F_{3,51}$=4.25, p<0.01
	Interaction due to resin v high dose	p<0.05
	Higher 'wellbeing' 60 minutes post dosing	$F_{1,51}$=23.2, p<0.001
Before dosing	No differences between doses	
25-mins after dosing	Significant differences	$F_{3,51}$=8.7, p<0.01
	Placebo v high dose	p<0.01
	Resin v high dose	p<0.01
	Placebo v low dose	p<0.05
	Resin v low dose	p<0.01
60-mins after dosing	Significant differences	
100-mins after dosing	Significant differences	

Table C5 Summary of analysis for 'dry mouth' question

Comparison	*Significant differences*	*Test statistic*
Over time – compared to before dosing	'Drier mouth' 25 minutes post dosing	$F_{1,51}$=75.2, p<0.001
	Interaction between dose and time at 25 minutes	$F_{3,51}$=5.08, p<0.01
	More listless 60 minutes post dosing	$F_{1,52}$=49.4, p<0.001
	More listless 100 minutes post dosing	$F_{1,52}$=25.3, p<0.001
Before dosing	No differences between doses	
25-mins after dosing	Significant differences	$F_{3,51}$=3.73, p<0.05
	Placebo (μ=33.1) v high dose (μ=61.5)	p<0.05
	Placebo (μ=33.1) v low dose (μ=62.1)	p<0.05

Analysis of willingness to drive

Responses to questions asking participants if they would be willing to drive were analysed separately. The results of the analyses are reported in Tables C6 to C8.

No significant differences for the willingness to drive for an *urgent reason*, between the different types of dosing, were observed at any time during the study.

Analysis of subjective effects and impairment

Responses to questions asking participants about the subjective effects they felt during the trial. These include the drug effect, feeling stoned, impairment and liking the effect being felt. The results of the analyses are reported in Tables C9 to C12.

A one-way ANOVA revealed significant differences of self-reported impairment, between the dosing types. Figures C4 and C5 illustrate the relationship with dose.

A one-way ANOVA revealed significant differences of the reported liking of the effect felt, between the dosing types.

Table C6 Summary of analysis for 'willingness to drive for an unimportant reason'

Comparison	*Significant differences*	*Test statistic*
Over time – compared to before dosing	'Less willing' 25 minutes post dosing	$F_{1,50}$=26.7, p<0.001
	Interaction between dose and time at 25 minutes	$F_{3,50}$=5.57, p<0.01
	'Less willing' 60 minutes post dosing	$F_{1,51}$=31.1, p<0.001
	Interaction between dose and time at 60 minutes	$F_{3,51}$=5.52, p<0.01
	'Less willing' 100 minutes post dosing	$F_{1,51}$=10.8, p<0.01
	Interaction between dose and time at 100 minutes	$F_{3,51}$=2.79, p<0.05
Before dosing	No differences between doses	
25-mins after dosing	Significant differences	$F_{3,51}$=3.22, p<0.05
60-mins after dosing	Significant differences	$F_{3,52}$=3.73, p<0.05
	Placebo (μ=74.4) v high dose (μ=39.5)	p<0.05

Table C7 Summary of analysis for 'willingness to drive for an important but unavoidable reason'

Comparison	*Significant differences*	*Test statistic*
Over time – compared to before dosing	'Less willing' 25 minutes post dosing	$F_{1,51}$=23.4, p<0.001
	Interaction between dose and time at 25 minutes	$F_{3,51}$=3.56, p<0.05
	'Less willing' 60 minutes post dosing	$F_{1,52}$=30.4, p<0.001
	Interaction between dose and time at 60 minutes	$F_{3,52}$=4.95, p<0.01
	'Less willing' 100 minutes post dosing	$F_{1,52}$=16.2, p<0.001
	Interaction between dose and time at 100 minutes	$F_{3,52}$=3.78, p<0.05
Before dosing	No differences between doses	
60-mins after dosing	Significant differences	$F_{3,52}$=3.54, p<0.05
	Placebo (μ=80.7) v high dose (μ=46.3)	p<0.05

Table C8 Summary of analysis for 'willingness to drive for an urgent reason'

Comparison	*Significant differences*	*Test statistic*
Over time – compared to before dosing	'Less willing' 25 minutes post dosing	$F_{1,51}$=16.6, p<0.001
	'Less willing' 60 minutes post dosing	$F_{1,52}$=26.1, p<0.001
	'Less willing' 100 minutes post dosing	$F_{1,52}$=18.7, p<0.001
	Interaction between dose and time at 100 minutes	$F_{3,52}$=3.07, p<0.05

Table C9 Summary of analysis for 'drug effect felt'

Comparison	*Significant differences*	*Test statistic*
Over time – compared to before dosing	'More effect' 25 minutes post dosing	$F_{3,52}$=13.7, p<0.001
	Placebo v low dose	p<0.001
	Placebo v high dose	p<0.001
	Placebo v resin dose	p<0.005
	'More effect' 60 minutes post dosing	$F_{3,52}$=7.59, p<0.001
	Placebo v low dose	p<0.001
	Placebo v high dose	p<0.001
	'More effect' 100 minutes post dosing	$F_{3,52}$=8.11, p<0.001
	Placebo v low dose	p<0.001
	Placebo v high dose	p<0.001

Table C10 Summary of analysis for 'feeling stoned'

Comparison	*Significant differences*	*Test statistic*
Over time – compared to before dosing	'More' 25 minutes post dosing	$F_{3,52}$=13.6, p<0.001
	Placebo (μ=17.4) v low dose (μ=56.9)	p<0.001
	Placebo v high dose (μ=64.4)	p<0.001
	Placebo v resin dose (μ=44.8)	p<0.01
	'More' 60 minutes post dosing	$F_{3,52}$=10.51, p<0.01
	Placebo v low dose	p<0.001
	Placebo v high dose	p<0.001
	Placebo v resin dose	p<0.05
	'More' 100 minutes post dosing	$F_{3,52}$=7.35, p<0.001
	Placebo (μ=13.5) v low dose (μ=45.8)	p<0.01
	Placebo v high dose (μ=50.9)	p<0.01
	Placebo v resin dose (μ=31.5)	p<0.05

Table C11 Summary of analysis for 'self-reported impairment'

Comparison	*Significant differences*	*Test statistic*
Over time – compared to before dosing	'More' 25 minutes post dosing	$F_{3,52}$=8.64, p<0.001
	Placebo (μ=12.9) v low dose (μ=34.9)	p<0.01
	Placebo v high dose (μ=48.2)	p<0.001
	High v resin dose (μ=26.5)	p<0.05
	'More' 60 minutes post dosing	$F_{3,52}$=9.51, p<0.01
	Placebo (μ=11.1) v low dose (μ=36.2)	p<0.001
	Placebo v high dose (μ=47.0)	p<0.01
	High v resin dose (μ=20.2)	p<0.01
	'More' 100 minutes post dosing	$F_{3,52}$=9.18, p<0.001
	Placebo (μ=4.7) v low dose (μ=30.5)	p<0.01
	Placebo v high dose (μ=34.9)	p<0.001
	High v resin dose (μ=13.0)	p<0.05

Table C12 Summary of analysis for 'liking of the effect'

Comparison	*Significant differences*	*Test statistic*
Over time – compared to before dosing	'More' 25 minutes post dosing	$F_{3,52}$=7.65, p<0.001
	Placebo v low dose	p<0.01
	Placebo v high dose	p<0.01
	Placebo v resin dose	p<0.01
	'More' 60 minutes post dosing	$F_{3,52}$=5.8, p<0.01
	Placebo v low dose	p<0.05
	Placebo v high dose	p<0.01
	Placebo v resin dose	p<0.05
	'More' 100 minutes post dosing	$F_{3,51}$=10.3, p<0.001
	Placebo v low dose	p<0.001
	Placebo v high dose	p<0.001
	Placebo v resin dose	p<0.05

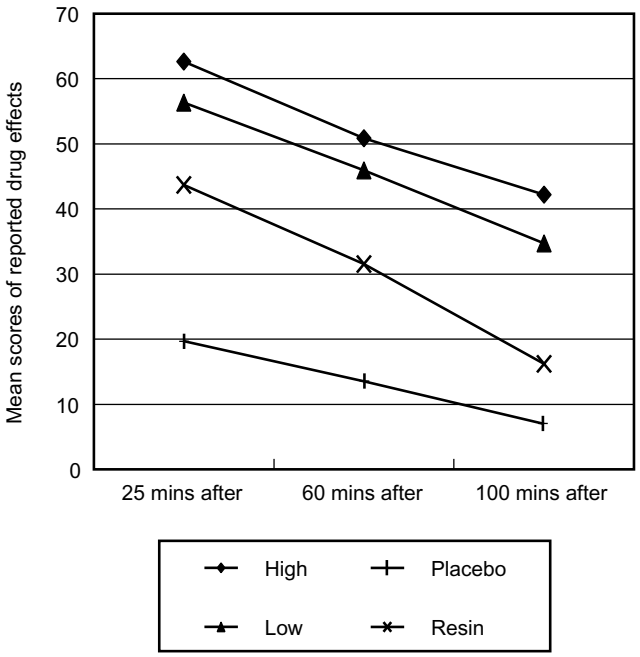


Figure C4 Mean scores of reported drug effect over time by dose type

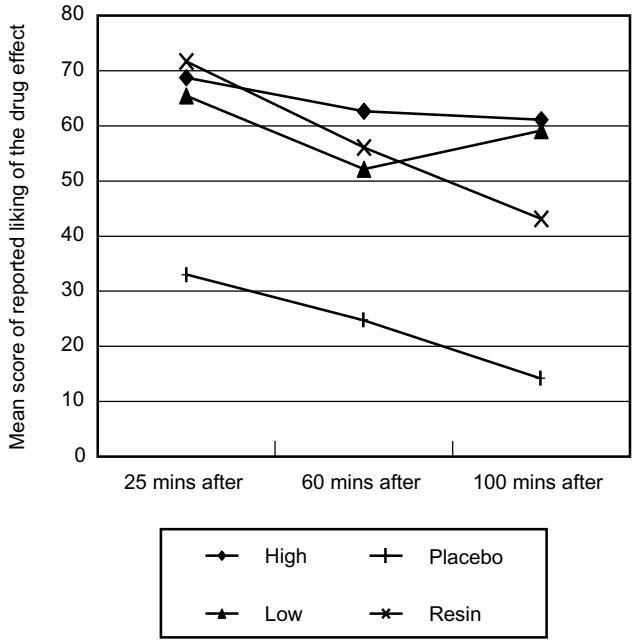


Figure C5 Mean scores of reported liking of the drug effect

Analysis of overall subjective effects and impairment

Participants were asked a set of four questions at the end of the study, concerning the overall drug effects and impairment. Post-hoc testing was carried out on the data. The analyses of the data are summarised in Table C13. Means scores are illustrated in Figure C6.

Discussion

In general, the results showed that with higher cannabis doses there was an increased level of anxiety and listlessness and a decrease in wellbeing. This was stronger just after dosing and decreased in effect as the effects wore-off. Participants reported a decrease in the drug effect over time, with the higher effects being associated with higher doses. They all reported a liking for the drug effect, but with higher doses were less willing to drive even 60 minutes after dosing.

Table C13 Summary of analysis for final questions at 100 minutes after dosing

Significant differences	*Test statistic*
Reported overall effect	$F_{3,52}$=19.33, p<0.001
Placebo v low dose	p<0.001
Placebo v high dose	p<0.001
Placebo v resin dose	p<0.01
High dose v resin dose	p<0.05
Overall liking of the drug	$F_{3,52}$=12.33, p<0.001
Placebo v low dose	p<0.001
Placebo v high dose	p<0.001
Placebo v resin dose	p<0.01
High dose v resin dose	p<0.05
The feeling of being stoned	$F_{3,52}$=19.68, p<0.001
Placebo v low dose	p<0.001
Placebo v high dose	p<0.001
Placebo v resin dose	p<0.001
The reported impairment	$F_{3,52}$=11.95, p<0.001
Placebo v low dose	p<0.001
Placebo v high dose	p<0.001
High dose v resin dose	p<0.05

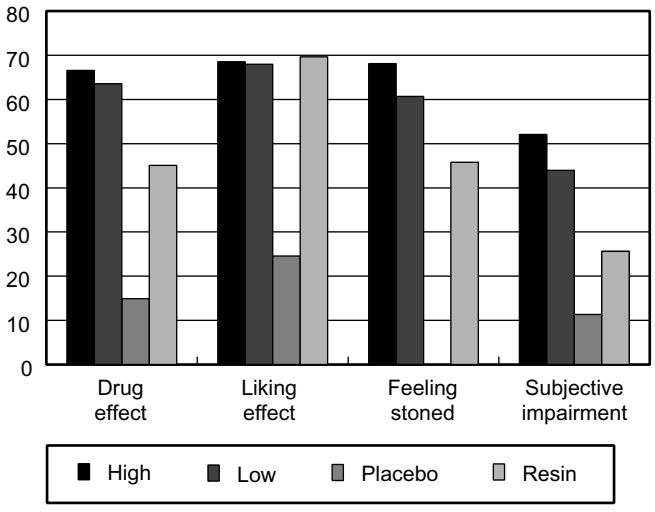


Figure C6 Mean scores of overall subjective drug effects

Appendix D: Screening document

C.1/99/TRL/UK

CASE REPORT FORM

SCREENING & CONSENT

Protocol number: C.1/99/TRL/UK

Subject number: ☐☐☐

Name of trial: Phase 1

Name: ☐☐☐
(first 3 letters of forename)

Centre: TRL

A DOUBLE BLIND, PLACEBO CONTROLLED, RANDOMISED, CROSSOVER STUDY OF THE EFFECTS ON DRIVING OF CANNABIS

Dates of visits: Visit 1 – Screening

day ☐☐ month ☐☐ year ☐☐

INVESTIGATORS

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Tel: 01344 773131

STUDY FLOW CHART

Summary of Study Design and Assessments

Treatments:
Placebo cannabis cigarette
Low THC dose cannabis cigarette
High dose cannabis cigarette
Self-rolled from supplied resin

Activity	screen	Treat 1	Treat 2	Treat 3	Treat 4
Demographic data/medical history	X				
Medical examination	X				
Urine sample	X	X	X	X	X
Blood haematology sample	X				
Baseline familiarisation drive	X	X	X	X	X
Baseline assessment drive		X	X	X	X
Baseline blood/saliva samples for THC		X	X	X	X
Visual analogue scales administration		X	X	X	X
Dosing - randomised		X	X	X	X
Blood/saliva samples for THC		X	X	X	X
Police impairment assessment tests		X	X	X	X
Visual analogue scales administration		X	X	X	X
Blood/saliva samples for THC		X	X	X	X
Driving tasks		X	X	X	X
Visual analogue scales administration		X	X	X	X
Psychometric tests		X	X	X	X
Saliva sample for THC		X	X	X	X
Visual analogue scales administration		X	X	X	X
Medical check and then taxi home		X	X	X	X

EFFECT OF CANNABIS INTAKE ON DRIVING IMPAIRMENT
SUBJECT INFORMATION SHEET

Thank you for considering taking part in this study. The information given in this leaflet should help to explain the object of the study and give you an idea of what is going to happen. When you have read it you will be given the opportunity to ask further questions and discuss the study with the research worker. You will then be asked if you are prepared to take part and to fill in and sign the written consent form.

Why have we asked for your help?

There are many reports which state that after alcohol, cannabis is the most frequently detected drug found in driving casualties of road traffic accidents. There is, however, very little research demonstrating how cannabis impairs driving and at what levels of cannabis intake this impairment occurs. This study is being undertaken to answer these questions.

How long will it last?

The study itself will be spread over 4-6 weeks. Each participant will be asked to attend a test session lasting approximately two hours and there are four separate test sessions, at least one week apart.

What will I have to do?

Participants will be asked to attend test sessions after consenting to the conditions outlined in the information sheet and consent form. After completing a questionnaire which assesses their drug use and driving history, the participant will be examined by a Doctor to ensure suitability to undertake the study.

If eligible to enter the study, each participant will be assigned at each visit to one of four different groups.

The groups are as follows:

- Placebo
- Low Cannabis Dose
- High Cannabis Dose
- Cannabis cigarette rolled by Participant (using supplied source of resin)

Each participant will undergo analysis of blood, urine and saliva at different times during the two hour testing procedure. During this two hour testing procedure the

participant will undergo different tests including driving a virtual reality computer based driving simulator.

At the end of each two hour testing procedure, the participant will be taken home by taxi.

What tests will be done?

Other than completion of several different questionnaires the table below gives a timetable of the different tests which will be undertaken during the two hour testing study period. This testing procedure is the same for each of the four groups and will, therefore, be repeated on four separate occasions.

Completion time (mins) from arrival	**Activity**
0	Arrival and urine sample
10	Baseline familiarisation on driving simulator
15	Baseline assessment of driving
20	Baseline blood/saliva samples
20	Questionnaire on mood/physical symptoms
30	Administration of cannabis
40	Blood/saliva samples
55	Impairment assessment tests as used by Police surgeons
55	Questionnaire on mood/physical symptoms
60	Blood/saliva samples
75	Driving simulator tests
80	Driving simulator tests
90	Driving simulator tests
90	Questionnaire on mood/physical symptoms
105	Video/PC based test of hazard perception
120	PC based reaction time tests
125	Saliva sample
130	Questionnaire on mood/physical symptoms
135	Medical examination and taxi home

Legal Issues

The Transport Research Laboratory is licenced to store cannabis on site and its use is covered by this licence.

Confidentiality Issues

All information relating to using is encrypted in order to ensure confidentiality.

Further caution is taken with regard to your confidentiality in that all information identifying you will be destroyed once payment for undertaking the study is achieved. We anticipate that this will be achieved approximately one week after the completion of the study.

What happens if I do not wish to continue the study?

Your participation in this study is entirely voluntary and all information received is treated as confidential. Even after you have agreed to take part, you are free to leave the study at any time and for any reason without prejudice to your medical care.

How do I get further information?

If you have any further questions about the study, talk to the Research Worker in charge. You can talk to him or her at any time during this study.

Thank you for your co-operation and help which is much appreciated.

WRITTEN CONSENT FORM

EFFECT OF CANNABIS ON DRIVING PERFORMANCE
(The subject should complete the whole of this sheet himself)

	Please delete as appropriate
Have you read the Subject Information Sheet?	**Yes** / **No**
Have you had an opportunity to ask questions and discuss this study?	**Yes** / **No**
Have you received satisfactory answers to all your questions?	**Yes** / **No**
Have you received enough information about the study?	**Yes** / **No**

Do you understand that you are free to withdraw from the study:

- at any time
- without having to give reason for withdrawing
- and without affecting your future medical care? **Yes** / **No**

You should only agree to take part in this study when all your answers to the above questions are 'YES'

Do you agree to take part in this study? **Yes** / **No**

Subject Name:.....

Signature:.....
.....

Date:.....

Principal Investigator's

Name:..... **Signature:**.....

Date:.....

Date			Subject		
day	month	year	number	name	Period
					S

SCREENING VISIT

Time of arrival: _____

Subject checks:

Criteria description	Include if	✓ If OK
Gender	male	
Age	≥18 and ≤ 60	
Car driver	for >12 months	
Cannabis user	for >12 months	
Cannabis frequency	at least weekly for 12 months	
Alcohol user	for >12 months	
History of substance abuse disorder (not nicotine)	none	
Medication	none	
Respiratory disorder	none	
Medical history	normal	
Height = _____cm & weight = _____Kg	in normal range	
Physical examination	in normal range	
12 lead ECG	in normal range	
Blood haematology and biochemistry tests (reference to laboratory analysis)	in normal range	
Visual acuity – via Snellen test	acceptable	
Prepared to commit to trial, (after reading subject information sheet)	positive	
Signed consent for trial	prepared to give	

Date			Subject		
day	month	year	number	name	Period S

Initial screening blood, and urine samples

Please take:

- Blood sample for haematology and biochemistry analysis.
- A urine sample in a sterile container

Blood taken ? Y/N _____

Urine sample obtained ? Y/N _____

Samples taken by: .....

Time: .....

Comments:

Date			Subject		
day	month	year	number	name	Period S

Self-completion questionnaire

Time statrted: _____ finished: _____

Checked by: _____

Completed sucessfully: Y/N _____

QUESTIONNAIRE A

Where appropriate please tick the appropriate box

Age ☐☐ years

1. Do you smoke normal (nicotine) cigarettes? yes ☐ no ☐ (Go to Q4)

2. On average approximately how many cigarettes do you smoke per day? ☐☐

3. What brand of cigarettes do you usually smoke? .....

4. Have you ever smoked cannabis, or not? yes ☐ no ☐ (Go to Q10)

5. At what age did you first start smoking cannabis? ☐☐ years

6. How often have you smoked cannabis in the past 6 months?

   i) every day ☐ ii) 2-6 days per week ☐ iii) once a week ☐

   iv) approximately once a fortnight ☐ v) approximately once a month ☐

   vi) less frequently ☐ *Please State* .....

7. For how long have you smoked cannabis at this frequency? For the past:

   i) 1 month ☐ ii) 6 months ☐ iii) 12 months ☐

   iv) more than 12 months ☐ *Please state* .....

8. Do you smoke: Joints? no ☐ yes ☐ weekly/monthly/less frequently(delete)

   Pipes? no ☐ yes ☐ weekly/monthly/less frequently(delete)

   Chillims? no ☐ yes ☐ weekly/monthly/less frequently(delete)

9. In general how many *joints* do you smoke on each occasion?
(If joints are generally shared, give an approximate answer)

i) Less than one ☐ ii) one ☐ iii) two ☐ iv) three ☐

v) more than three ☐ *Please state* .....

10. Do you drink alcohol, or not? yes ☐ no ☐ (Go to Q15)

11. How often do you drink alcohol?

i) every day ☐ ii) 2-6 times per week ☐

iii) once a week ☐ iv) once a fortnight ☐

vi) once a month ☐ vii) less frequently ☐ *Please state* .....

12. Approximately how many units of alcohol *per week* do you drink?

☐☐ units

13. Approximately how many units of alcohol *per occasion* do you drink?

☐☐ units

14. Do you ever drink alcohol and take cannabis together? yes ☐ no ☐ (Go to Q15)

If yes, how often?

i) every day ☐ ii) 2-6 times per week ☐

iii) less frequently ☐ *Please state* .....

15. How long have you been driving? .....

16. Do you drive at least twice a week? yes ☐ (Go to Q17) no ☐

If no, approximately how often do you drive? .....

17. Do you ever drink *more* than 4 units of alcohol on any occasion and drive?
(a unit of alcohol is about half-pint of beer, a glass of wine or a single measure of spirits)

i) at least once a week ☐ ii) at least once a month ☐

iii) less than once a month ☐ *Please state* ..... iv) never ☐

18. Do you ever drink *less* than 4 units of alcohol and drive?

i) at least once a week ☐ ii) at least once a month ☐

iii) less than once a month ☐ *Please state* ..... iv) never ☐

19. Do you ever smoke cannabis at the same time as you are driving?

i) at least once a week ☐ ii) at least once a month ☐

iii) less than once a month ☐ *Please state* ..... iv) never ☐

20. Do you ever drive after smoking cannabis?

i) at least once a week ☐ ii) at least once a month ☐

iii) less than once a month ☐ *Please state* ..... iv) never ☐

21. Have you ever had alcohol, and then smoked cannabis, and then driven? yes ☐ no ☐ (Go to Q22)

If yes, then how often?

i) at least once a week ☐ ii) at least once a month ☐

iii) less than once a month ☐ *Please state* .....

Do you generally drink *less* than 4 units of alcohol on these occasions?
yes ☐ no ☐

22. Do you smoke cannabis alone or socially?

i) alone ☐ ii) socially ☐ iii) both ☐

23. Do you believe that drinking *4 or more* units of alcohol affects your driving performance? Would you say that your driving is:

i) very much impaired ☐ ii) slightly impaired ☐

iii) not at all impaired ☐ iv) improved ☐

State whether you answer this question on the basis of experience or by estimation (i.e. at a guess).

i) experience ☐ ii) estimation ☐

24. Do you believe that being *high* on cannabis affects your driving performance? Would you say that your driving is:

i) very much impaired ☐ ii) slightly impaired ☐

iii) not at all impaired ☐ iv) improved ☐

State whether you answer this question on the basis of experience or by estimation (i.e. at a guess).

i) experience ☐ ii) estimation ☐

If impaired, for how long after smoking your last joint do you think that your performance is affected?
(If your answer depends on how much you have smoked, please state the minimum and maximum amount of time, e.g. from x mins to x hours)

.....

25. If you believe your driving is altered by the effects of cannabis, describe below how you think it is affected. What sort of experiences, difficulties or advantages does using cannabis have on driving?

.....

.....

.....

.....

.....

.....

26. If you plan to drive home after a social cannabis-smoking situation, do you deliberately smoke less cannabis? yes ☐ no ☐

27. If you drove to a party with no intention of smoking cannabis, but were offered some cannabis, would you:-

a) refuse, and drive home later ☐

b) get high, and drive home later ☐

c) smoke a small amount, not get high, and drive home later ☐

d) get high, and not drive ☐

e) get high, but wait until the effects had worn off before driving ☐

f) none of these, I never drive after a party ☐ (Go to Q29)

28. If you were to also drink alcohol at the party, but less than 4 units, would that change your answer to question 27? yes ☐ no ☐ (Go to Q 29)

If yes, would it change to: a) ☐ b) ☐ c) ☐ d) ☐ e) ☐

29. Do you ever attempt to counteract the effects of cannabis and/or alcohol before driving (e.g. drinking coffee)? yes ☐ no ☐ (Go to Q30)

If yes, what do you do? .....

.....

30. Do you take any other drugs such as ecstasy, cocaine, amphetamine (speed), LSD?

yes ☐ no ☐ (Go to Q31)

If yes, then what drugs do you take and how often?

..... weekly/monthly/less frequently (delete)

..... weekly/monthly/less frequently (delete)

..... weekly/monthly/less frequently (delete)

31. Have you ever taken cannabis in food or liquid form?

yes ☐ no ☐ (Go to Q32)

If yes, then in what form have you taken it (e.g. cakes)? .....

.....

Did you enjoy it? yes ☐ no ☐

32. Have you ever been stopped by the police while driving under the influence of alcohol? yes ☐ *Please state age(s):* ..... ☐ no (Go to Q33)

If yes, were you charged? yes ☐ no ☐

What was the penalty? .....

Has this acted as a deterrent? yes ☐ no ☐

33. Have you ever been stopped by the police while driving under the influence of drugs (any drugs)? yes ☐ *Please state age(s):* ..... ☐ no

If yes, were you charged? yes ☐ no ☐

What was the penalty? .....

Has this acted as a deterrent? yes ☐ no ☐

Date			Subject		
day	month	year	number	name	Period
					S

Screening familiarisation drive on simulator

Was the subject happy with the simulator drive Y/N ? _____

Time completed drive _____

Administered by: .....

If the subject was unhappy with his familiarisation drive then consult with the study investigators.

Screening baseline drive on simulator

(The baseline drive consists of left and right-handed curves.)

Was the subject happy with the drive Y/N ? _____

Time completed drive: _____

Administered by: .....

Outcome variables: Standard Deviation of left-hand curve: _____

Standard Deviation of right-hand curve: _____

Outcome variables supplied by: .....

Comments:

Date			Subject		
day	month	year	number	name	Period S

Screening familiarisation on Hazard perception test

Was the subject happy with the HP test Y/N ? _____

Time completed _____

Administered by: .....

Result of screening

Check	pass	fail
Inclusion criteria		
Blood haematology in normal range		
Urine samples confirms a cannabis user		
Interview showed an acceptable subject		
Simulator familiarisation and baseline measure		
All medical checks		
Prepared to be part of study		
	accept	**reject**
DECISION		

Completed by: .....

Date: .....

Data Input

Data input by: .....

Date: .....

Data input checked by: .....

Appendix E: Case report form

C.1/99/TRL/UK

CASE REPORT FORM

Periods 1 – 4

Protocol number: C.1/99/TRL/UK

Subject number: ☐☐☐

Name of trial: Phase 1

Name: ☐☐☐
(first 3 letters of forename)

Centre: TRL

A DOUBLE BLIND, PLACEBO CONTROLLED, RANDOMISED, CROSSOVER STUDY OF THE EFFECTS ON DRIVING OF CANNABIS

Date of visits:

Visit date — day ☐☐ month ☐☐ year ☐☐

Period (1,2, 3 or 4) _____

In the event of premature discontinuation

Subject withdrawn on: ☐☐ ☐☐ ☐☐

Trial discontinued on: ☐☐ ☐☐ ☐☐
day month year

INVESTIGATORS

Mr B Sexton/Dr R Tunbridge
Transport Research Laboratory
Old Wokingham Road, Crowthorne
Berkshire RG45 6AU
Tel: 01344 773131

STUDY FLOW CHART

Summary of Study Design and Assessments

Treatments:
Placebo cannabis cigarette
Low THC dose cannabis cigarette
High dose cannabis cigarette
Self rolled joint

Activity	screen	Treat 1	Treat 2	Treat 3	Treat 4
Demographic data/medical history	X				
Medical examination	X				
Urine sample	X	X	X	X	X
Blood haematology sample	X				
Baseline familiarisation drive	X	X	X	X	X
Baseline assessment drive		X	X	X	X
Baseline blood/saliva samples for THC		X	X	X	X
Visual analogue scales administration		X	X	X	X
Dosing - randomised		X	X	X	X
Blood/saliva samples for THC		X	X	X	X
Police impairment assessment tests		X	X	X	X
Visual analogue scales administration		X	X	X	X
Blood/saliva samples for THC		X	X	X	X
Driving tasks		X	X	X	X
Visual analogue scales administration		X	X	X	X
Psychometric tests		X	X	X	X
Saliva sample for THC		X	X	X	X
Visual analogue scales administration		X	X	X	X
Medical check and then taxi home		X	X	X	X

Trial day activity timetable:

Completion time (mins) from arrival	Responsibility	Activity
0	Sue/Kay	Arrival, BAC check test
10	Sue	Baseline familiarisation drive
15	Sue	Baseline assessment – lateral deviation on curve
20	Nurse	Baseline blood/urine/saliva samples
20	Kay	Visual analogue scales administration
30	Kay	Dosing
40	Nurse	Blood/saliva samples
55	Margaret/Karen	Police impairment assessment tests
55	Kay	Visual analogue scales administration
60	Nurse	Blood/saliva samples
75	Sue	Simulation reaction time tests
80	Sue	Simulation lateral deviation on curve tests
90	Sue	Simulation reaction to traffic lights turning green
90	Kay	Visual analogue scales administration
105	Kay	Hazard perception test
120	Kay	CTT+ test
125	Nurse	Saliva sample
130	Kay/Nurse	Post trial questions
135	Nurse/Sue/Kay	Medical check and then taxi home

MINOR ADVERSE EVENT FORM

Please complete one adverse event form for each event the patient experiences.

Date of assessment: .....

ADVERSE EVENT Description (signs and symptoms)	Severity 1) Mild 2) Moderate 3) Severe	Date of Onset			Time to Onset If <24 hrs after 1st dose	Outcome 1) Resolved 2) Improved 3) Unchanged 4) Worse	Duration if resolved
		Day	Month	Year			

Overall diagnosis (where possible)

Action taken: .....

.....

.....

Comments: .....

.....

.....

CAUSALITY	Almost certainly	Probably	Possibly	Unlikely	Unrelated
Do you think the adverse event was related to the study treatment?					

Date of assessment: .....

ADVERSE EVENT Description (signs and symptoms)	Severity 1) Mild 2) Moderate 3) Severe	Date of Onset			Time to Onset If <24 hrs after 1st dose	Outcome 1) Resolved 2) Improved 3) Unchanged 4) Worse	Duration if resolved
		Day	Month	Year			

Overall diagnosis (where possible)

Action taken: .....

.....

.....

Comments: .....

.....

.....

CAUSALITY	Almost certainly	Probably	Possibly	Unlikely	Unrelated
Do you think the adverse event was related to the study treatment?					

SERIOUS ADVERSE EVENT FORM – CONFIDENTIAL

Please complete an adverse event form for each serious event the patient experiences.

Date of assessment: .....

1. PATIENT DETAILS							
Date of Birth:	Patient Identification			Sex:	Male		Female

2. ADVERSE EVENT Description (signs and symptoms)	Severity 1) Mild 2) Moderate 3) Severe	Date of Onset			Time to Onset If <24 hrs after 1st dose	Outcome 1) Resolved 2) Improved 3) Unchanged 4) Worse	Duration if resolved
		Day	Month	Year			

Overall diagnosis (where possible)								
Was the event life-threatening to this patient? Yes		No						
3. TREATMENT OF ADVERSE EVENT: to resolution	No	Yes			No	Yes	If yes, time	
Study drug withdrawn?			If yes, did symptoms resolve?				Mins. Hrs. Days	
Did the event require								
Hospitalisation?			If yes, give details					
Prolongation of hospitalisation?			If yes, give details					
Drug treatment?			If yes, give details					

4. CAUSALITY	Almost certainly	Probably	Possibly	Unlikely	Unrelated
a) Could patient's original condition or other illness account for adverse event?					
b) Do you think the adverse event was related to study treatment?					

5. COMMENTS	
6. RESEARCH ASSOCIATE	Signature:
Name (please print)	Date:

Date			Subject		
day	month	Year	number	name	Period

PERIOD .....

Time of arrival: _____ **location: waiting area**

Initial subject checks:

	correct	incorrect
The subject is the expected subject		
Subject has not drunk caffeine within the past 2 hours		
Subject has not drunk alcohol within the past 12 hours		
Subject is not taking medication		
Subject appears lucid		
BAC alcohol check is OK i.e. not significant BAC reading		
Subject is content to proceed with the trial		

If any of the responses are incorrect then consult with the study investigators before proceeding.

Familiarisation drive on simulator

location: simulator area

Time started drive _____

Was the subject happy with the simulator Y/N ? _____

Administered by: .....

If the subject was unhappy with his familiarisation drive then consult with the study investigators before proceeding.

Date			Subject		
day	month	year	number	name	Period

Baseline drive on simulator

(The baseline drive consists of left and right-handed curves and follows on from the familirisation drive, the subject then drives to two traffic light controlled junctions)

Was the subject happy with the drive Y/N ? _____

Time completed drive: _____

Administered by: .....

Outcome variables: Standard Deviation of left-hand curve: _____

Standard Deviation of right-hand curve: _____

Outcome variables supplied by: .....
Comments:

If the subject was unhappy with his baseline drive then consult with the study investigators before proceeding.

Date			Subject		
day	month	year	number	name	Period

Pre-dosing blood, urine and saliva samples

Location - blood sampling room

Before dosing please take:

- blood for THC and THC metabolite analysis.
- A saliva sample
- A urine sample in a sterile container

Blood taken ? Y/N _____

Saliva taken? Y/N _____

Urine sample obtained ? Y/N _____

Samples taken by: .....

Time: .....

Comments:

Date			Subject		
day	month	year	number	name	Period

Visual Analogue Scale – pre-dosing

Time started: ..... **Location: smoking room**

Please answer all the following questions by placing a vertical mark through the line for each item. Mark the lines according to how you feel at this moment.

Cheerful

Not at all _____ extremely

Confident

Not at all _____ extremely

Clearheaded

Not at all _____ extremely

Calm

Not at all _____ extremely

Tense

Not at all _____ extremely

Alert

Not at all _____ extremely

Drowsy

Not at all _____ extremely

Date			Subject		
day	month	year	number	name	Period

Anxiety

Absent _____ Severe

Sweating

Absent _____ Severe

Shaking or Trembling

Absent _____ Severe

Palpitations

Absent _____ Severe

Nausea or Sickness

Absent _____ Severe

Dizziness

Absent _____ Severe

Irritability

Absent _____ Severe

Loss of Appetite

Absent _____ Severe

Physical Tiredness

Absent _____ Severe

Slow Movements

Absent _____ Severe

Difficulty Concentrating

Absent _____ Severe

Date			Subject		
day	month	year	number	name	Period

Dry Mouth

Absent _____ Severe

Increased Heart-rate

Absent _____ Severe

Increased Bodily Awareness

Absent _____ Severe

Difficulty Remembering

Absent _____ Severe

How willing would you be to operate a motor vehicle for an unimportant though gratifying reason? (e.g. drive friends to a party)

Not at all _____ extremely

How willing would you be to operate a motor vehicle for an important, but avoidable reason? (e.g. driving a friend home, who feels mildly ill, when they could get a taxi)

Not at all _____ extremely

How willing would you be to operate a motor vehicle for an urgent reason? (e.g. driving a severely sick child to hospital)

Not at all _____ extremely

Responses taken by: .....

Time completed: .....

Date			Subject		
day	month	year	number	name	Period

Dosing with cannabis cigarette

Location – smoking room

The subject should sit in the 'dosing' room and smoke the supplied joint in the manner described to him.

Treatment reference number from humidifier:		
Was the correct subject number on the humitifier?	Y	N
Did the subject smoke the joint as required?	Y	N
Did the subject self-titrate?	Y	N
Time started smoking		
Weight of joint before smoking:		
Time completed smoking		
Weight of joint after smoking:		

Supervised by: .....

Comments:

Date			Subject		
day	month	year	number	name	Period

---

10 minutes post-dosing - blood and saliva samples

Time started: ..... **Location: blood sampling room**

Exactly 10 minutes after smoking started please take:

- 10mls blood for THC and THC metabolite analysis.
- A saliva sample

Blood taken ? Y/N _____

Saliva taken? Y/N _____

Samples taken by: .....

Time completed: .....

Comments:

CANNABIS STUDY MEDICAL EXAMINATION FORM

General examination

General demeanour and behaviour:	Normal	Euphoric	Anxiety	Verbosity
	Sedation	Hallucination		
State of clothing:	Normal			
Speech: (ask "Have you been well over the last week?")	Normal	Slurred		
Condition of mouth:	Normal			
Pulse: rate and character		b.p.m.	Normal	Bounding
Temperature:		^{o}C		
State of tongue:	Normal			
Breath:	Normal			
Ears:	Normal	Wax	TM Red	
Heart:	Normal			
Blood pressure:				
Lungs (added sounds):	Normal	Wheeze		
Reflexes:	Normal	Increased	Decreased	
Eyelids red or swollen?	Normal			
Conjunctivae?	Normal	Injected		
Evidence of squint etc?	Normal			
Any gross visual defect?	Normal			
Glasses?	Yes	No		

Impairment testing

Pupil size (using card pupillometer)		mm
Anisocoria	Absent	Present
Pupillary reaction to direct light stimulus	Normal	Sluggish
Horizontal gaze nystagmus	Absent	Present
Vertical gaze nystagmus	Absent	Present
Convergence	Present	Absent

Walk and turn test (9 steps)	Start too soon	Yes	No
	Stops walking	Yes	No
	Misses heel/toe	Yes	No
	Raises arms	Yes	No
	Starting balance	Impaired	Normal
	Turns improperly	Yes	No
	Steps off line	Yes	No
	Correct step count	Yes	No
	Fails instructions	Yes	No

		Right		Left	
One leg stand	Sways	Y	N	Y	N
	Raises arms	Y	N	Y	N
	Hops	Y	N	Y	N
	Puts foot down	Y	N	Y	N
	Fails instructions	Y	N	Y	N

Finger nose test (eyes closed)	Touch tip of nose	Yes	No
Left / Right / Left / Right / Right / Left	Correct hand	Yes	No
	Sways	Yes	No
	Fail instructions	Yes	No

Romberg test - body sway	Yes	No

Internal clock - 30 seconds estimates at		Time
(allow 10 seconds either way)	Normal	Abnormal

Writing: copy this

1.Remarks (include any unsolicited remarks regarding volunteer's feelings)

2.Conclusion

Impaired?	Yes	No
Condition might be due to a drug?	Yes	No

Date			Subject		
day	month	year	number	name	Period

Visual Analogue Scale – 25 minutes post-dosing

Time started: ..... **Location – meeting room**

Please answer all the following questions by placing a vertical mark through the line for each item. Mark the lines according to how you feel at this moment.

Cheerful

Not at all _____ extremely

Confident

Not at all _____ extremely

Clearheaded

Not at all _____ extremely

Calm

Not at all _____ extremely

Tense

Not at all _____ extremely

Alert

Not at all _____ extremely

Drowsy

Not at all _____ extremely

Date			Subject		
day	month	year	number	name	Period

Anxiety

Absent _____ Severe

Sweating

Absent _____ Severe

Shaking or Trembling

Absent _____ Severe

Palpitations

Absent _____ Severe

Nausea or Sickness

Absent _____ Severe

Dizziness

Absent _____ Severe

Irritability

Absent _____ Severe

Loss of Appetite

Absent _____ Severe

Physical Tiredness

Absent _____ Severe

Slow Movements

Absent _____ Severe

Difficulty Concentrating

Absent _____ Severe

Date			Subject		
day	month	year	number	name	Period

Dry Mouth

Absent _____ Severe

Increased Heart-rate

Absent _____ Severe

Increased Bodily Awareness

Absent _____ Severe

Difficulty Remembering

Absent _____ Severe

How willing would you be to operate a motor vehicle for an unimportant though gratifying reason? (e.g. drive friends to a party)

Not at all _____ extremely

How willing would you be to operate a motor vehicle for an important, but avoidable reason? (e.g. driving a friend home, who feels mildly ill, when they could get a taxi)

Not at all _____ extremely

How willing would you be to operate a motor vehicle for an urgent reason? (e.g. driving a severely sick child to hospital)

Not at all _____ extremely

Date			Subject		
day	month	year	number	name	Period

Please answer all the following questions by placing a vertical mark through the line for each item. Mark the lines according to how you feel at this moment.

How strong is the drug effect you feel now?

Not at all _____ extremely

How much do you like the drug effect now?

Not at all _____ extremely

How stoned on cannabis are you now?

Not at all _____ extremely

How impaired is your performance?

Not at all _____ extremely

Responses taken by: .....

Time completed: .....

Date			Subject		
day	month	year	number	name	Period

25-35 minutes post-dosing - blood and saliva samples

Time started: ..... **Location - blood sampling room**

25-35 minutes after dosing please take:

- 10mls blood for THC and THC metabolite analysis.
- A saliva sample

Blood taken ? Y/N _____

Saliva sample taken? Y/N _____

Samples taken by: .....

Time completed: .....

Comments:

Date			Subject		
day	month	year	number	name	Period

Simulator assessment drive (45 mins post dosing)

Time started drive: ..... **Location – simulator hall**

Simulation tasks	**Completed (Y/N)**
1. Motorway drive for reaction times	
2. Figure of 8 for 'wobblyness'	
3. Traffic light scenario	
	Outcome measures
M'way 'pulling-out' reaction time – Event 1 (1/100thsec)	
Event 2	
Event 3	
Event 4	
Event 5	
M'way braking traffic reaction times – Event 1 (1/100th sec)	
Event 2	
Event 3	
Figure of 8 - Standard Deviation of left-hand curve	
Standard Deviation of right-hand curve	
Traffic light – time to start at 1st set of lights (secs to 1/100th)	
time to start at 2nd set of lights	
time to start at 3rd set of lights	
time to start at 4th set of lights	

Time completed drive: _____

Administered by: .....

Outcome measures supplied by: .....
Comments:

Date			Subject		
day	month	year	number	name	Period

Visual Analogue Scale – 60 minutes post-dosing

Time started: ..... **Location – meeting room**

Please answer all the following questions by placing a vertical mark through the line for each item. Mark the lines according to how you feel at this moment.

Cheerful

Not at all _____ extremely

Confident

Not at all _____ extremely

Clearheaded

Not at all _____ extremely

Calm

Not at all _____ extremely

Tense

Not at all _____ extremely

Alert

Not at all _____ extremely

Drowsy

Not at all _____ extremely

Date			Subject		
day	month	year	number	name	Period

Anxiety

Absent _____ Severe

Sweating

Absent _____ Severe

Shaking or Trembling

Absent _____ Severe

Palpitations

Absent _____ Severe

Nausea or Sickness

Absent _____ Severe

Dizziness

Absent _____ Severe

Irritability

Absent _____ Severe

Loss of Appetite

Absent _____ Severe

Physical Tiredness

Absent _____ Severe

Slow Movements

Absent _____ Severe

Difficulty Concentrating

Absent _____ Severe

Date			Subject		
day	month	year	number	name	Period

Dry Mouth

Absent _____ Severe

Increased Heart-rate

Absent _____ Severe

Increased Bodily Awareness

Absent _____ Severe

Difficulty Remembering

Absent _____ Severe

How willing would you be to operate a motor vehicle for an unimportant though gratifying reason? (e.g. drive friends to a party)

Not at all _____ extremely

How willing would you be to operate a motor vehicle for an important, but avoidable reason? (e.g. driving a friend home, who feels mildly ill, when they could get a taxi)

Not at all _____ extremely

How willing would you be to operate a motor vehicle for an urgent reason? (e.g. driving a severely sick child to hospital)

Not at all _____ extremely

Date			Subject		
day	month	year	number	name	Period

Please answer all the following questions by placing a vertical mark through the line for each item. Mark the lines according to how you feel at this moment.

How strong is the drug effect you feel now?

Not at all _____ extremely

How much do you like the drug effect now?

Not at all _____ extremely

How stoned on cannabis are you now?

Not at all _____ extremely

How impaired is your performance?

Not at all _____ extremely

Responses taken by: .....

Time completed: .....

Date			Subject		
day	month	year	number	name	Period

Hazard Perception test - 75 minutes post-dosing

Time started: ..... **Location: Impairment test area**

Hazard perception tape number	
Test completed (Y/N)	
Reaction time to 1st hazard	
to 2nd hazard	
to 3rd hazard	
to 4th hazard	
to 5th hazard	
Spotted 1st potential hazard (Y/N)	
2nd potential hazard	
3rd potential hazard	
4th potential hazard	
5th potential hazard	

Data taken from PC screen and printed copy made for audit reference.

Responses taken by: .....

Printed version made? Y/N _____

Subject reference written on paper copy? Y/N _____

Time completed: .....

Date			Subject		
day	month	year	number	name	Period

CTT test - 90 minutes post-dosing

Time started: ..... **Location: Impairment test area**

(There are 18 practice trials and 72 real trials.)

Test completed (Y/N)	
No. of correct trials	
No. of incorrect trials	
Mean tracking accuracy	
Standard error of tracking accuracy	
Mean response time	
Standard error of response time	

Data taken from PC screen.

Responses taken by: .....

Time completed: .....

Date			Subject		
day	month	year	number	name	Period

---

95 minutes post-dosing - saliva samples

Time started: ..... **Location - blood sampling room**

95 minutes after dosing please take:

- A saliva sample

Saliva taken? Y/N _____

Sample taken by: .....

Time completed: .....

Comments:

Date			Subject		
day	month	year	number	name	Period

Final questionnaire - 100 minutes post-dosing

Time started: ..... **Location – meeting area**

Please answer all the following questions by placing a vertical mark through the line for each item. Mark the lines according to how you feel at this moment.

Cheerful

Not at all _____ extremely

Confident

Not at all _____ extremely

Clearheaded

Not at all _____ extremely

Calm

Not at all _____ extremely

Tense

Not at all _____ extremely

Alert

Not at all _____ extremely

Drowsy

Not at all _____ extremely

Date			Subject		
day	month	year	number	name	Period

Anxiety

Absent _____ Severe

Sweating

Absent _____ Severe

Shaking or Trembling

Absent _____ Severe

Palpitations

Absent _____ Severe

Nausea or Sickness

Absent _____ Severe

Dizziness

Absent _____ Severe

Irritability

Absent _____ Severe

Loss of Appetite

Absent _____ Severe

Physical Tiredness

Absent _____ Severe

Slow Movements

Absent _____ Severe

Difficulty Concentrating

Absent _____ Severe

Date			Subject		
day	month	year	number	name	Period

Dry Mouth

Absent _____ Severe

Increased Heart-rate

Absent _____ Severe

Increased Bodily Awareness

Absent _____ Severe

Difficulty Remembering

Absent _____ Severe

How willing would you be to operate a motor vehicle for an unimportant though gratifying reason? (e.g. drive friends to a party)

Not at all _____ extremely

How willing would you be to operate a motor vehicle for an important, but avoidable reason? (e.g. driving a friend home, who feels mildly ill, when they could get a taxi)

Not at all _____ extremely

How willing would you be to operate a motor vehicle for an urgent reason? (e.g. driving a severely sick child to hospital)

Not at all _____ extremely

Date			Subject		
day	month	year	number	name	Period

Please answer all the following questions by placing a vertical mark through the line for each item. Mark the lines according to how you feel at this moment.

How strong is the drug effect you feel now?

Not at all _____ extremely

How much do you like the drug effect now?

Not at all _____ extremely

How stoned on cannabis are you now?

Not at all _____ extremely

How impaired is your performance?

Not at all _____ extremely

Please answer all the following questions by placing a vertical mark through the line for each item. Mark the lines according to how you feel at this moment.

How strong was the drug effect overall?
Not at all _____ extremely

How much did you like the drug effect overall?
Not at all _____ extremely

How stoned on cannabis were you?
Not at all _____ extremely

How impaired was your performance during the testing period?
Not at all _____ extremely

Date			Subject		
day	month	year	number	name	Period

Final check before departing by taxi

Location – Doctor's room

Final subject checks:

	correct	incorrect
The subject is lucid		
Blood pressure: ..... checks OK?		
Pulse rate: ..... OK?		
Subject is not complaining about being unwell		
Subject has been advised about not driving nor operating heavy machinery within next 3 hours?		
Subject understands that he must attend next week (unless 4th period)		
Subject has been paid and initialed sheet (only if 4th period)?		
Subject is content to be taken home		

If any of the responses are incorrect then consult with the study investigators before letting him leave in the taxi.

Responses taken by: .....

Departure time: .....

Data Input

Data input by: .....

Date: .....

Appendix F: Home Office licence

Licence No. **99/DM5/7152**
File No. **DDA 99 4600/1/1**

MISUSE OF DRUGS ACT 1971

LICENCE TO BE IN POSSESSION

In pursuance of the Misuse of Drugs Act 1971 (hereinafter called 'The Act'), the Secretary of State hereby grants to
TRANSPORT RESEARCH LABORATORY

(hereinafter called 'the licensee'): at:

OLD WOKINGHAM ROAD
CROWTHORNE
BERKSHIRE
RG45 6AU

a licence to have in its possession the drug(s) listed in the schedule overleaf, including any stereoisomeric forms, and the salts thereof and any preparation or other product containing any proportion of the drug(s) or its/their salts (hereinafter called 'the drug(s)), subject to the following conditions:

1. The drug(s) shall be used by the licensee for the sole purpose of a research project to evaluate the effects of cannabis inhalation on driving.

2. The licence permits the smoking of delta 9 THC and cannabis resin solely by the participants in the research project referred to in condition 1 and only at the premises named above.

3. The delta 9 THC should only be obtained from Dr Terry, School of Psychology, University of Birmingham, Edgbaston, Birmingham, B15 2TT, and the cannabis resin from HM Customs and Excise.

4. The licence shall be produced on demand to the person or company from whom any supply of the drug(s) is obtained.

5. All stocks of the drug(s) shall at all times be in the charge of the licensee or some responsible servant appointed by the licensee for the purpose.

6. The licensee shall keep a record of all amounts of the drug(s) coming into its possession in pursuance of this licence, showing in respect of each amount the date when received, the quantity received, the form in which received and the name and address of the person or company from whom received. Likewise the licensee shall keep a record of all amounts of the drug(s) used showing in respect of each amount the date when used and the quantity and form in which used. These entries shall be made on the day on which the drug(s) is/are received or used, as the case may be, or, when that it not reasonably practicable, on the following day. Where this licence authorises the licensee to have in its possession more than one drug, a separate record shall be kept for entries made in respect of each of the drugs. These records shall be kept on the premises to which they relate, preserved for a period of at least two years from the date on which the last entry is made, and produced on the demand of a constable or an inspector of the Home Office Drugs Branch.

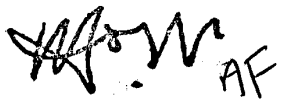
7. The licensee shall furnish to the Secretary of State such returns of the amounts of the drug(s) in its possession or coming into its possession in pursuance of this licence, and of its use of the same, as may from time to time be required.

8. The licensee shall report any thefts or losses of the drug(s) from the address named above as soon as possible to a constable and, by giving notice in writing to that effect to the Chief Inspector, Drugs Branch, Home Office, 50 Queen Anne's Gate, London SW1H 9AT, to the Secretary of State.

9. The licence is valid only for the licensee, and in respect of the address named above. In the event of the licensee ceasing to carry on business or to be employed or otherwise engaged at this address, or if the authority of the licence is revoked by the Secretary of State, the licensee shall return the licence immediately to the address below.

10. The licence and any stocks of the drug(s) shall be produced for inspection when required by a constable or an inspector of the Home Office Drugs Branch.

This licence, unless sooner revoked, shall continue in force until **31st October 2000.**



HEAD OF DIVISION

HOME OFFICE
DRUGS BRANCH
50 QUEEN ANNE'S GATE
LONDON
SW1H 9AT

Date: **14th December 1999**

F:\KO141692.AADU

NOTES

1. Under Section 18 of the Act it is an offence for the licensee to contravene a condition of this licence.

2. Regulation 26 of the Misuse of Drugs Regulations 1985 imposes requirements regarding the destruction of drugs.

SCHEDULE OF DRUGS

CANNABIS RESIN

DELTA-9-TETRAHYDROCANNABINOL

HM CUSTOMS AND EXCISE
Detector Dog Service (DDS)
Bowman House, 100-102 Talbot Street, Nottingham NG1 5NF

Telephone: 0115 971 2121/2118 Fax: 0115 948 3487

Mr Roger Peal
Head of Road Safety Division
Department of the Environment
Transport and the Regions
Zone 2/14
Great Minster House
76 Marsham Street
London, SW1P 4DR

Our ref: DTS 01/2000

21st January 2000

Dear Mr Peal

ISSUE OF DRUG DOG TRAINING SAMPLES
AUTHORISATION NUMBER:- DTS 01/2000

With reference to your Department's phone call today. I am pleased to confirm that you are authorised to receive a further supply of the following samples for use in your research project relating to the influence of cannabis on driving:-

Drug Sample	Quantity & Size
Cannabis Resin:	20 grams

Samples are issued from Heathrow Airport Queen's Warehouse and you should contact Mrs Vijay Kapila on 0181 910 3660 to confirm availability of the samples and a convenient time for collection. A copy of this letter should be produced on collection together with a copy of the Home Office licence.

Once collected, the drug samples become entirely the responsibility of yourselves. This includes storage, security and eventual destruction. We would remind you that the samples should never be passed to a third party and steps should be taken to guard against loss, misappropriation, adulteration or dilution of purity.

Yours sincerely

J. Margaret Denham
Detector Dog Service

cc Mrs Vijay Kapila, Q.W. Heathrow
DDS File

Received as above.

H.M. CUSTOMS & EXCISE
QUEEN'S WAREHOUSE
26 JAN 2000
CUSTOM HOUSE
LONDON AIRPORT NORTH
HOUNSLOW, MIDDX

Abstract

The results from a study of different doses of cannabis and the influence on driving and driving related skills are reported. The study required participants who were male, drivers and regular cannabis users to undertake a variety of different tasks. The participants were given cannabis to smoke, either in the form of a prepared grass-based cannabis cigarette or were asked to prepare a typical joint to smoke using supplied cannabis resin. The prepared 'grass' based cannabis cigarettes were supplied by NIDA (National Institute on Drug Abuse) and varied in active THC content to give a placebo, a low dose and a high dose. Each participant attended four test sessions where they were given a different cannabis dose, the dose ordering was fully randomised for the NIDA cigarettes. The participants drove the TRL simulator on a motorway, a 'figure of eight' and a dual carriageway with traffic light controlled junctions. Various measures of their driving skill were taken. They also took a test of their hazard perception and a compensatory tracking task. They also underwent sobriety testing 10-15 minutes after dosing and completed a mood questionnaire at different times during their test session. Three blood samples and four saliva samples were taken. On arrival urine was screened for polydrug use and a breathalyser test was administered to exclude recent alcohol consumption. The blood and saliva samples were analysed for different components of cannabis.

Related publications

TRL464 *Recognising drug use and drug related impairment in drivers at the roadside* by R J Tunbridge, M Keigan and F J James. 2000 (price £25, code E)

TRL226 *Validation trial for testing impairment of driving due to alcohol* by B F Sexton. 1997 (price £25, code E)

RR202 The incidence of drugs in road accident fatalities by J T Everest, R J Tunbridge and B Widdop. 1989 (price £20, code A)

SR441 *A review of drinking and drug taking in road accidents in Great Britain* by B E Sabey. 1978 (price £20)

CT42.2 Alcohol, drugs and driving update (1996-1998) *Current Topics in Transport: selected abstracts from TRL Library's database* (price £20)

CT97.1 Injuries from traffic accidents update (1998-2000) *Current Topics in Transport: selected abstracts from TRL Library's database* (price £20)

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